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GUIDE LINES FOR MANUSCRIPT PREPARATION

1. **Title Page** should contain: concise and informative title, Name(s) of the author(s) with initials and surname, name of the department, Institution & complete address with telephone number and e-mail of the corresponding author.

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Original Research Article

Effectiveness of Structured Teaching Program on Knowledge of First aid Management of Minor Injuries Among Mothers of Kinder Garten Students of SPA Campus Bhauri, Bhopal

Satly Shaju
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ABSTRACT

Quasi- Experimental one group pretest –post test design was conducted to assess the effectiveness of structured teaching program on first aid management of minor injuries among mothers of kindergarten children at bhauri.60 samples were selected by simple random sampling technique and assessed their knowledge score by structured questionnaire. Structured teaching program on first aid management of minor injuries were given .After seven days of the post test were conducted by using same questionnaire. There was significant improvement in knowledge score and practices related to prevention of minor abrasions at 0.01 level. Out of 60 mothers 3.3%(2) had adequate knowledge, 13.4%(8) had moderately adequate knowledge, 83.3%(50) had inadequate knowledge score in pre-test. 1.66 %(1) had inadequate knowledge, 86.7 %(52) had adequate knowledge, 11.64 %(7) had moderately adequate knowledge in post test..there is no significant difference between demographic variables of pre test and post test scores of knowledge and knowledge on practice.

KEY WORDS: assess, first aid, knowledge

INTRODUCTION:

Adequate knowledge required for handling injuries in mothers of kindergarten students without hospital setting (home or site of accidents) may not be sufficient as formal first aid training is not given to them . Imparting knowledge on first aid management could help in preventing injuries and also to deal with the injuries caused more effectively[1]. Minor injuries in children are common these injuries can result in scar formation which could adversely affect even their personality. Knowledge in first aid management prevents such instances to great extend.

Need of the study:

From the Indian context it can be said that all children have experienced minor injuries due to fall. The recent studies have revealed that knowledge level of parents or even the teachers to deal with these injuries are inadequate and some cases have resulted in disabilities. Adequate knowledge on this management of injuries can help the parents to deal with them and also to take a decision for secondary assistance from the hospital. The knowledge on the reasons for fall and the nature of injuries resulting from such fall will help to wear protective gear and educate the children on the consequences of fall. Awareness in the parents will enable them to give timely first aid or required treatment effectively[2].

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Statement of Problem:

A study to assess the effectiveness of structured teaching program on knowledge of first aid management of minor injuries among mothers of kinder garten students residing SPA Campus Bhauri at Bhopal.

Objectives of the Study:

1. To assess the pre existing knowledge score on first aid management among the mothers of kinder garden students (children below 5 years of age).
2. To evaluate the effectiveness structured teaching program by comparing pretest &post test knowledge score.
3. To find out the association between pretest knowledge score of first aid management and selected demographic variables.

Hypotheses:

H_1: There will be difference between pre and post test level of score on knowledge of first aid management among the mothers of kinder garten students at the level of $p<0.05$.

H_2:There will be significant association between knowledge of first aid management among mothers of kinder garten students and selected Demographic variables at the level of $p<0.05$.

Research Methodology:

Research approach : Evaluative approach
Research Design : Quasi- experimental research design
Setting : SPA campus
Population : Mothers of kinder garden children in SPA campus
Sampling technique : Simple random sampling technique
Sample size : 60

Inclusion criteria:
The mothers of kinder garten students are willing for the study. Mothers are available at the time of the study.

Exclusion criteria: Mothers are not willing for the study; *Research Tool*: Structured questionnaire.

Data collection Procedure:

The Investigator introduced herself to the mothers and explained the significance of the study. Consent was obtained from them after explaining them the purpose of the study. The questions are administered and responses are obtained and recorded in pre test and 45 minutes Structured teaching program was imparted to the group. After seven days of structured teaching program the post test conducted.

RESULTS:

Section-I distribution of demographic variables among mothers. Majority of the mothers (33%) were studied up to Primary school, followed by High school (14%) and above (3%) and only few of them (50%) were Illiterate. Only few of the students' fathers (5%) were labourer while Majority of them (59%) was Farmer, followed by Businessman (28%) and Employee (8%).Only few of the mothers (2%) were employee while majority of them (40%) were home maker, followed by Labourer (56%) and remaining (4%) were doing business.

Section-II: Distribution of level of knowledge and knowledge on practice related to prevention of minor injuries among mothers in pre test and post test. Out of 60 mothers Very few parents (10%) had received knowledge relating to first aid from their teachers, followed by friends (12%), health professionals (12%), Family members (27%), and mass media (39%). Over all knowledge on minor injuries and knowledge on practices indicated 68% had poor knowledge and 32% had inadequate knowledge in pre-test.

Majority of the respondents (70%) had average knowledge and remaining (30%) had good knowledge in the post test as compared to the pre test where majority (68%) had poor knowledge and remaining (32%) had average knowledge. The mean post test knowledge score ($X_{2=}$ 22.10) was apparently higher than the mean pre test knowledge score ($X_{1=}$ 11.12) suggesting that Structured teaching program was effective in increasing the knowledge of the students on first aid.

Table: Comparing of Pretest &Post test knowledge score.

Pre-test knowledge score			Post-test knowledge score		
Poor	Average	Good	Poor	Average	Good
68%	32%	0	0%	70%	30%

DISCUSSION:

The study revealed that out of 60 mothers 68% had poor knowledge and 32% had Average knowledge in pretest. 70% had average knowledge and 30% had good knowledge on knowledge score on first aid management among the mothers of kinder garden students. There is a significant improvement in knowledge and knowledge practices related to prevention of minor injuries at 0.01 levels and there is no significant difference between demographic variables of pretest and post test scores of knowledge and knowledge on practice. Research hypothesis was accepted. This result clearly shows that was useful in improving the knowledge of mothers on first aid for selected accidents and emergencies[3]. Therefore it was confirmed that structured teaching program was an effective strategy to improve the knowledge level of the mothers.

The findings have its support from the following studies:

According to a study on effectiveness of planned teaching program on first aid among 60 high school students of Udupi, India, it showed that there was a significant difference between the mean pre test and post test knowledge scores of the High School

children for selected accidents and emergencies (t_{60}=13.41, p<0.05)[4].

A quasi-experimental study was adopted to assess the effect of structured teaching program on First Aid Management and Emergency Care of burn patients among 60 staff nurses working in selected hospitals of Ludhiana, Punjab. The study revealed that the maximum pre-test knowledge score of staff nurses in control group (56%) and experimental group (60%) was good[5]. Maximum post-test knowledge score in control group was good (52%) while in experimental group, it was excellent (96%) .

Recommendation: On the basis of finding of the study, the following recommendation is made for the future research study[6]. A similar study can be replicated with broader content area on accidents and emergencies. A comparative study can be conducted between urban and rural schools and college. A similar study can be replicated with different demographic variables. A similar study can be replicated with different population[7].

Implication: Immediate first aid during emergency situation helps to sustain the life and prevent complication. Training program in these areas will help to develop the skills of the community. In this context, health professional especially nurses has a major role in training the community, by using the most effective and simplest method. The nursing curriculum should lay more emphasis on first aid. The students posted in the community health, school health, hospital should be able to give education to the people regarding first aid.

CONCLUSION:

There is a significant difference in pre and post level of knowledge regarding first aid management minor injuries. This showed that the planned teaching program was effective in increasing the knowledge of mothers regarding first aid management of minor injuries.

Ethical Clearance:

Prior permission was obtained from the Registrar of SPA .informed consent was obtained from the samples .confidentiality and privacy of the data was maintained.

Source of fund: Self.
Conflict of interest: None.

REFERENCES:

1. Mohan D. Childhood injuries in India extend of the problem and strategies for control. Indian J Pediatr. 1986; 53: p 607 – 9.
2. Park K. text book of preventive and social medicine 19th ed. Jabalpur: Banarasidas Bhanot; 2007:340 – 5.
3. Report of School Health Committee, Ministry of Health, Government of India. 1991.
4. St. John Ambulance Association in India. First Aid to the Injured. 12th ed. Thane; T.G. Bhave publishers; 2015
5. American Heart Association and the American National Red Cross. Circulation. 2005 13th Dec. http://www.circu-lationaha.org
6. Suresh KP, Chandrashekara S. Sample size estimation and power analysis for clinical research studies. J Hum Reprod Sci. 2012; 5(1): 7–13. doi: 10.4103/0974-1208.97779
7. Treece EW, Treece JW. Elements of research in nursing 2nd End.; Saint Louis: CV. Mosby; 1997.

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A Study to Assess the Effectiveness of Balloon Therapy on Lung Capacity of Patients with Lower Respiratory Tract Infections in Selected Hospital of Chitrakoot U.P.

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Original Research Article

ABSTRACT

Respiratory disease is a significant chronic health problem in community. Respiratory disease is the most distressful conditions, badly affecting in human life. Respiratory system is a frequent site of illness in adults. Respiratory infection and allergies together are responsible for many disruptions in family life.

The main aim of the study was to assess the effectiveness of balloon therapy on respiratory status of patients with lower respiratory tract disorders. Quasi experimental design was used for this study. Balloon therapy need to improve pulmonary function committing to a daily routine of blowing up 10 balloons will steadily increase lung capacity. The data pertaining to lung capacity was collected using self-administered questionnaire and respiratory assessment vital, tidal and lung capacity were done using balloon therapy. Among 50 patients, 13 (26%) patients have acute lung capacity, 21 (42%) patients had moderate lung capacity, 16 (32%) patients had severe lung capacity score before the implementation of balloon therapy whereas after the implementation of balloon therapy, 20 (40%) patients had normal score in COPD, acute and chronic bronchitis and pneumonia (100%) attained normal lung capacity. The result of this study proved that regular practice of balloon therapy can improve the lung capacity to a greater extent among patients with lower respiratory tract infection.

KEY WORDS: balloon therapy, respiratory disease, lower respiratory tract infections, lung capacity

INTRODUCTION:

Healthy adults brought up in healthy surrounding are not only source of joy work to everyone, but also India's greatest resource tomorrow. They are in a dynamic process of growth and development, and are particular vulnerable to acute and chronic effects of pollutants in their environment, which lead to disease like respiratory tract infections, COPD, acute and chronic bronchitis and asthma.

Adults respond differently to respiratory illness. The respiratory changes that occur during smoking, pollution and other work, lung tissue continues to form and existing structure change in shape and function. However, most respiratory condition is more stressful for adults, more often leading to airway obstruction or respiratory failure. Acute infection of the lower respiratory tract may be diagnosed in adults.

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Objectives of the Study

1. To assess the lung capacity of patients before balloon therapy on patients with lower respiratory tract infections.
2. To assess the lung capacity of patients after balloon therapy on patients with lower respiratory tract infections.
3. To compare the lung capacity before and after balloon therapy on patients with lower respiratory tract infections.

Hypothesis:

H1: There is a significant difference between the pretest and post test level of lung capacity among patients with lower respiratory tract infections.

Assumptions:

1. Patients with lower respiratory tract infection may have ineffective breathing pattern.
2. The balloon therapy will be effective on lung capacity of patients with lower respiratory tract infections.
3. Balloon therapy is easy to perform, cost effective and have beneficial effects on lung capacity.

Operational Definitions:

- Effectiveness: In this study, changes in physiological breathing pattern in term of rate, rhythms it refers to the desired changes that can be brought about by balloon therapy on lung capacity of patients with lower respiratory tract infections.
- Balloon therapy: A simple exercise that is done by blowing up balloon each day for 30 minutes helps increasing lung capacity. In this study the patients encourage to inflate a new ordinary balloon at 10 times a day for 10 days.
- Lower respiratory tract infection: Lower respiratory tract infections (LRTIs) occurs when there is an infection of the lungs, specifically in the lower airway, lung, bronchi and alveolus.

Research Methodology:

Approach: Quantitative research approach
Independent variable: Balloon therapy
Dependent variable: Lung capacity
Setting: District Hospital chitrakoot (UP)
Accessible Population: The population included for this study were patients with lower respiratory tract infections admitted in District Hospital Chitrakoot (UP).
Sample size: 50
Sampling Technique: Purposive

Organization and Presentation of Data:

The data were collected, organized and presented under the following section
Section I: Socio-Demographic Variables
Section II: Lung Capacity of patients before and after Balloon therapy.
Section I: Socio-Demographic Variables

Table 1: Distribution of subjects according to age patients (N=50).

Age	Frequency	Percentage
20 – 30 years	12	24%
31-40 years	17	34%
41-50 years	21	42%
Total	50	100%

Table 1 and Figure 1 represent that Majority of Patients i.e. 21 (42%) were in between the age group of 41to 50 years, 17 (34%) were in between 31-40 years of age and 12 (24%) were in 20-30 years of age with lower respiratory tract infections**.**

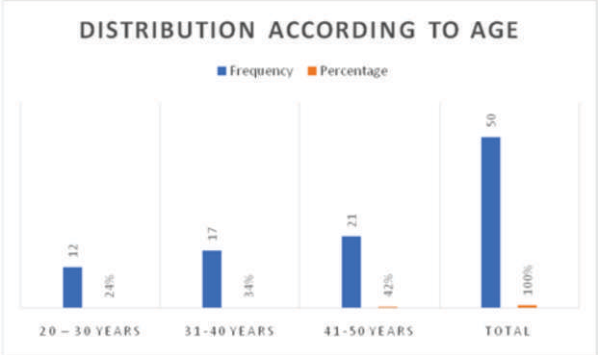

Figure 1: Showing represent that Majority of Patients.

Table 1 and Figure 1 represent that Majority of Patients i.e. 21 (42%) were in between the age group of 41to 50 years, 17 (34%) were in between 31-40 years of age and 12 (24%) were in 20-30 years of age with lower respiratory tract infections**.**

Table 2: Distribution of frequency and percentage of patients according to Gender (N = 50).

Gender	Frequency	Percentage
Male	45	90%
Female	5	10%
Total	50	100%

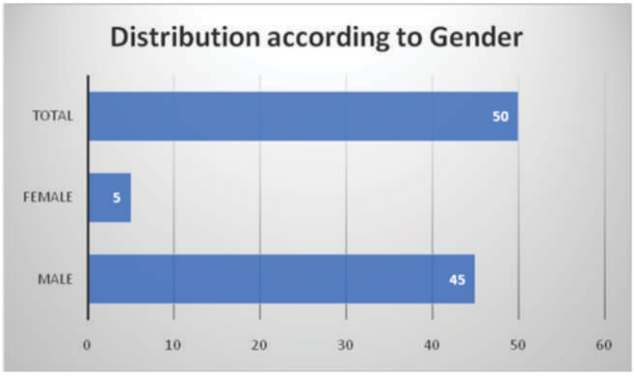

Figure 2: Showing lower respiratory tract infections**.**

Table 2 & Figure 2 Depicts that out of 50,45 patients (90%) were males and 5 patients (10%) were females with lower respiratory tract infections.

Table 3: Distribution of frequency and percentage of patients according to any previous disease.

Any previous disease	Frequency	Percentage
Yes	15	30%
No	35	70%
Total	50	100%

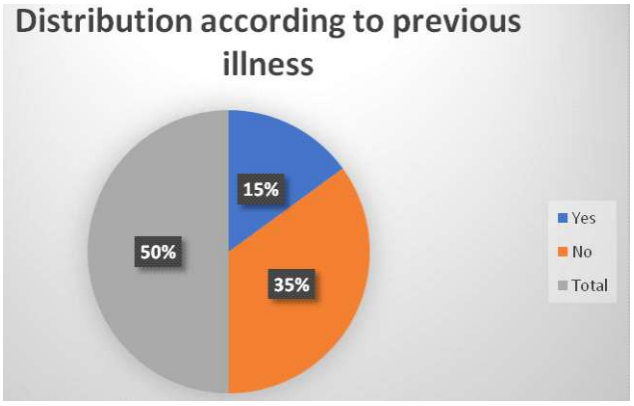

Figure 3: Showing distribution according to previous illness.

Table 3 &Figure 3 Show that 35 (70%) were not having any previous disease while 15 (30%) had previous disease.

Table 4: Distribution of frequency and percentage of patients according to Habit (N=50).

Habit	Frequency	Percentage
Smoking and Alcohol	16	32%
Tobacco chewing	34	68%
Any others	0	0%
Total	50	100%

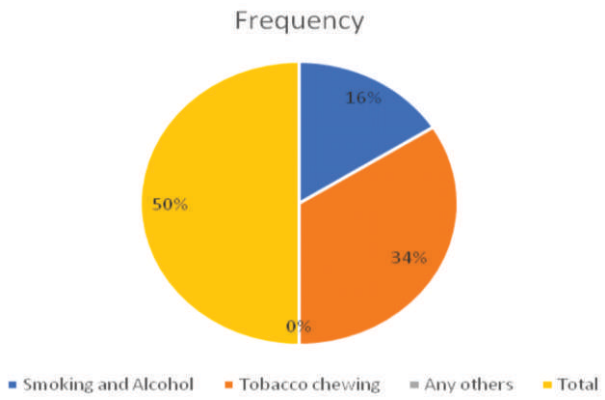

Figure 4: Represents patients habit of chewing tobacco.

Table 4 and Figure 4 represents 34 (68%) patients have the habit of chewing tobacco, 16 (32%) have the habit of Alcohol intake and were smokers.

Table 5 and Figure 5 describe that pre-test mean and SD were 6.83 & 1.30 respectively whereas post test mean & SD were 7.16 & 1.26, with t-test value of 6.12 and tabulated value at 0.001. These reading indicate the effectiveness of Balloon therapyon lung capacity inpatients with lower respiratory tract infections.

Section II & Table 5: Analysis of Difference Between Pre-Test and Post-Test Lung Capacity.

	Mean	SD	t test value	df	Tabulated value	Significant
Pre test	6.8300	1.30576	6.129	49	2.00	Significant at p value 0.05
Post test	7.1620	1.26812				

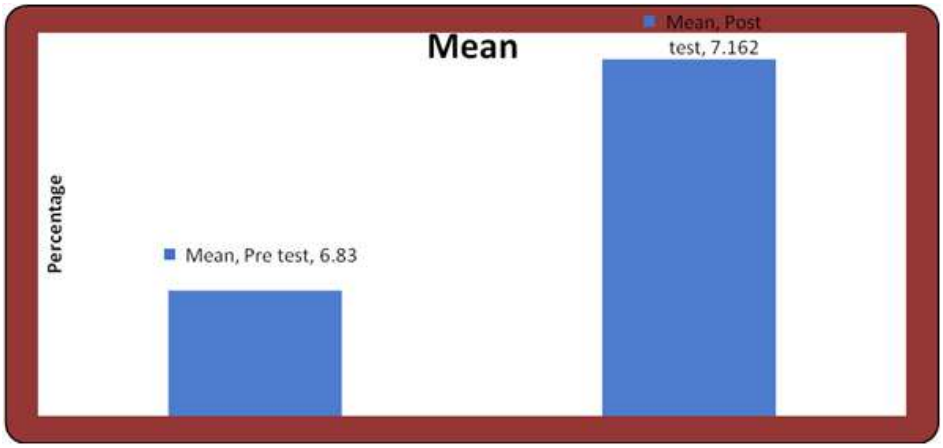

Figure 5: Describe that pre-test mean and SD.

Implications:

Nursing Practice:

In Nursing practice, Nurse can teach patients regarding effectiveness of balloon therapy.

Nursing services department can arrange health education program for teaching patients regarding balloon therapy.

Nursing Education

Nursing students must be encouraged to utilize their knowledge on promotive measure by health education and demonstration in hospital.

Nursing Administration

Administrators should take initiative action to update the knowledge of nursing personnel regarding breathing exercise in improvement of lung function and reducing the sign of respiratory illness by in-service education.

Nurse administrators can conduct workshop and seminar on breathing exercise for lower respiratory tract to all level of nursing personnel in the hospital.

Nursing Research

Evidence based practice helps the nurses to enrich them in knowledge and practice. Nursing researcher should be directed to toward exploring the advantages of balloon therapy so that the lung capacity can be improved.

REFERENCES:

1. Brunner & Siddarth's, Medical Surgical Nursing, 10th Edn.; Lippincott publications. 2004; pp: 513-633.
2. Block JM. Medical Surgical Nursing Clinical management of positive outcome, 6th Edn.; 1st Volume, Elsevier publication. 2004);pp: 1651-1746.
3. Jaya J. Essential of Respiratory Care. 5th End;. New Delhi; Jaypee brothers medical publisher; 2007. pp.78-79.
4. R Nielsen. M Klemmetsby M, Economics of COPD. National Institute of Health. 2008; 13(5). pp 429-434
5. Sharma SK. Textbook of Nursing Research and statistics. 3rd Edn.; New Delhi: Elsevier India Pvt.Ltd;2014; pp.80-82.
6. Sharma S. A Textbook of Nursing Research and Statistics, 3rd End.; New Delhi: Jayvee Brothers Medical Publisher. 2011; pp.101.

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Hepatitis & Nanomedicine: A Review

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Review Article

ABSTRACT

In the year 1989, hepatitis C virus (HCV) was specifically established as causative factor accountable for many more occurrences of hepatitis. It's a chronic disease which majorly contributes to Carcinoma and Cirrhosis. The hepatitis C virus belongs a family Flaviviridae (+) enveloped ssRNA virus. It has been described seven major genotypes of HCV and their subtypes (a, b). Around 3 percent among global residents has been infected by HCV. HCV Transmission is frequently associated with direct percutaneous blood contact, via blood transfusions, health-related injections and substance use injections. Several new therapies have been developed to treat HCV, such as polyethylene glycol (PEG)-ylated interferon / ribavirin, antivirals acting directly and antivirals targeting the host. Despite progress in anti-HCV therapy, there is still a urgent need for new approaches of targeted drug delivery systems using nanomedicine which are affordable and reliable. Nanotechnology has the ability to play a pivotal role in lowering viral load levels and drug-resistant HCV by targeting drugs directly to the disease site. In addition to tissue targeting, a wide variety of drugs need to be administered intracellularly to achieve a therapeutic effect in the organ affected. The contribution of nanoparticles as a promising delivery mechanism for HCV immunizing, diagnostic and therapeutic agents and there latest developments of drug carriers as well as their role in anti-HCV therapy were addressed in this review.

KEY WORDS: hepatitis c virus, flaviviridae, antivirals, interferon, nanotechnology

INTRODUCTION:

In the beginning of 21st century, two viruses (hepatitis A and hepatitis B), are major causative factors for hepatitis. While it was authenticated as early as 1950 for the third form of hepatitis, it wasn't till 1970, when blood examinations related to HAV, HBV became accessible, that the new agent referred to as non-A, non-B hepatitis (NANBH) has been recognized [1]. It became clear after the launch of the HBV blood test; NANBH is accountable for hepatitis[2]. Sufficient research work has been carried out with respect to isolation of this virus along with its therapy also. HCV came to be recognized as main factor for NANBH, was recognized as silent pandemic. HCV was found in the year 1988. Laboratory tests have been valid for detecting HCV infections since 1989[3-4]. HCV is a major human pathogen borne in the blood. Approximately 3% global residents has been HCL infected. As per WHO data, about 30 to 40 lakh new infections has been annually reported[5-6]. HCV has been identified as a main health related trouble, which can further leads to Cirrhosis, Carcinoma. In advanced all region, intravenous substance misuse is the most effective route for HCV transmission, while in developing region injection therapy causes new infections[7]. Major infections lead to chronic conditions without treatment, accompanied with cirrhosis and HCC. Misuse of alcohol and dysmetabolic syndrome are the primary co-factor affecting advanced liver disease and HCC development[8]. Approximately 30 percentages of liver transplants are performed annually in persons with HCV-related problems, with decompensated cirrhosis or HCC[9]. The concern of hepatitis C is projected to increase in the next decade because of the aging of the currently infected population[10-11]. During this time, the number of HCV-related cases of cirrhosis is expected to increase by 31% and HCC by around 50% [10] with an additive effect due to the incidence of the metabolic syndrome[12-13]. HCV infection is therefore a significant public health problem that should be resolved through strong policy measures aimed at efficiently detecting and treating patients infected with HCV. Seven genotypes (gt 1-7), and several HCV subtypes are

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there. The rate of infection and the prevalence of the subtype are dependent on the region. In less and more endemic countries, the gap between the infection rate is around 20 percent[14-15]. For example, the HCV prevalence is the lowest in North America, Western North Europe and Australia. In comparison, the prevalence of the virus is high in Asian and African countries. Egypt has reported the highest prevalence of viruses, where 22 percent of the population is infected [16]. It was postulated that during the period of parenteral-anti-schistosomal mass treatment campaigns prior to 1985, the outbreak was triggered by widespread iatrogenic transmission[17].

Virology:

HCV is a RNA virus with a positive-sense, single-stranded 9600 kb weight. A single HCV polyprotein of 3011 amino acids is translated in three structural proteins and seven non-structural proteins by the cellular and viral proteases[18]. Linked viral sequences in dogs[19], horses[20], rats, and bats[21] were identified. HCV infection in human populations display significant genetic variation, clarified in part by the long evolutionary relationship between the virus and humans[22]. Many studies have focused on first six genotypes HCV. All the genotypes are globally distributed, in African region 1, 2, 4 and 5 genotypes; in Asian region 3 and 6 genotypes has been distributed [23]. Medical initiatives related to schistosomiasis have been escalated in Egypt over the last century[24]. In United Kindom, genotype 3a is a coinfluenced trait of 1a genotype which has indications for vaccine therapy. In addition, HCV have immense genetical diverseness in contaminated carriers, which occurs as a swarm of associated quasi species in the blood. This diversity is the product of error-prone viral polymerase, and rapid viral multiplication allows rapid accommodation to the antibody response, cellular immune response and antiviral drugs[25]. HCV growth in tissue culture was not possible until a particular strain of the HCV genotype 2 was discovered[26]. HCV culture was used to classify a diverse collection of surface receptor interactions, including CD81, SCARB1 (a scavenger receptor) and two close junction proteins, OCLN and CLDN1[27]. These models allowed the creation of critical insights into viral multiplication and host – virus interactions [28]. Study using Electron microscopy reflected that mature viruses are having atypical structural arrangements[29]. Significantly, capability to study tissue culture HCV multiplication associated with structure related protein analysis which has led to the optimization of new unique DAAs[30-32].

Immunology:

Cell mediated immunological reactions to HCV influences consequences of acute illness along with the progression of lengthy illnesses. Acute immunological reactions to HCV include both innate branches of the immune system and adaptive ones. Polymorphic changes in IL28B gene have a strong influence on spontaneous infection resolution[33]. IFNL3 codes of interferon, lambda 3, which is having antiviral response same as response of interferon, but with limited receptoral distribution. It remains to be clarified whether polymorphisms recognized affect the control of IFNL3 or IFNL4[34]. Similarly, linkages between genes in the KIR (Killer cell immunoglobulin-like receptors) locus along with infection resolution reflects natural (killer) cell reactions plays an important role in virus associated regulation[35]. Acute host defense involves adaptive responses regulated with the help of CD8 cells and CD4 T cells. Many studies have reported more combinations via HLA class II alleles, along with good-powered genome-wide association case study[33]. Association of HLA class-I was recognized at single source epidemic[36]. CD4 cell mediated reaction and CD8 T-cell mediated reactions are necessary in complete safety of chimpanzees[37]. As a consequence of these kind of studies, there is a need to optimize T cell-based protective vaccines that is based on 2 recombinant vectors[38]. Also studied in detail were B cell responses to HCV, which lead to the generation of neutralizing antibodies[39]. The variability of regions such as the HCV E2 envelope protein hyper variable regions within hosts is a result of immune selection driven by anticorps. However, broadly cross-reactive neutralizing antibodies have been described[40] and further work to characterize these antibodies could lead to the development of antibody-based vaccines, particularly in the context of the recently described HCV E2 crystal structure[41].

Epidemiology:

HCV is most efficiently transmitted through percutaneous blood exposure/transfusion, organ transplantation (which may be infected previously) and injection use for medication purpose[42]. Exposure of mucosa with any blood or serum that makes transmission far less effective[43-44]. Transfusion via blood was a main cause behind HCV infection prior to testing and that transfusion mode was eliminated in regions where blood donator's screening generally conducted[45]. Drug use injection is the biggest risk factor in the United States and Australia, and accounts for most new diagnoses of HCV infection in Europe[42]. In addition to the sharing of needles, the sharing of other

things such as foil and spoons was involved in the transmission of HCV[46]. Transmission of sexual and perinatal HCV does occur but to a significantly lesser extent than with hepatitis B. Perinatal transmission in mothers co-infected with HIV occurs at a rate of about 4% and is two to four times higher[47]. As of today no proof present from randomly regulated testing for showing superiority of caesarean section against normal (vaginal) mode of delivery in maternity[48].

Ratio of transmission via sexual intercourse remains debatable; in normal hetero sexual associations rate is very minimal. Co-infection with HIV, relationship duration, or chronic liver disease may be independent cofactors that increase the risk of transmission[49]. Further sexual risk factors for transmission were indicated by data from a UK case-control study of acute HCV infection in men who have sex with men attending HIV clinics in three urban centres. Infection had been associated with permucosal rather than percutaneous transmission factors. Compared with controls, men with acute HCV had more sexual partners, showed increased sexual behaviour at high risk, and were more likely to have shared drugs in the previous year via a nasal or anal route. Sex was the strongest predictor of case or control status in a group of more than two people[50]. HCV along with HIV co-transfusion is a major health risk, with about 10% persons who are having HIV infection at the same time are also having infection of HCV globally[51]. In many advanced regions risk is from 25% to 50-95% in many risk sectors (though many HCV infected persons are not HIV infected)[52]. HIV infection is having major effect on the viral load of HCV infection[53] also on the clinically progression of a disease[54].

Chronic hepatitis C and it's pathophysiology:

This disease also not result of direct damage of liver cells via infection of HCV. Chronic hepatitis C generally results through intermediate immunological reaction which is large to enhance hepatocellular damage. This kind of immunological reaction is not sufficient to expell virus and culminates in fibrosis along with liver cirrhosis. In quantitative terms, in the chronic phase, HCV-specific CD4 reaction along with CD8 T-cell mediated reaction is weak as compared to acute phase of viral infection. Patients with poor acute response are often asymptomatic (no jaundice) and are more likely than those with high immune responses to become chronic carriers[55].

HCV specific CD8 cells have an impaired effector function (both the secretion of antiviral cytokines and lytic activity).

Clinical illustration:

Acute HCV disease is scientifically identical from many responses of acute viral hepatitis infection. That can cause high fever, muscular pain along with discomfort feeling sensations. Usually the acute phase is asymptomatic though. Following acute HCV infection, subsequent events vary significantly between patients but three patterns were noted:

- Ø Viral clearance (below blood detection level)
- Ø Viral durability without host regulation
- Ø Midway phase (virus is momentarily regulated along with recurrence)

Almost 80% HCV-infected persons leads to the chronic phase of viral infection which generally exists for minimum 180 days post viral onset. Infection rates vary by age, gender, ethnicity, HCV genotype and immune system status[56]. For example, HIV-infected patients are rapidly progressing to liver disease, whereas in West Africa, where genotype 2 infection predominates, the clearance rate is 50% due to the high frequency HLA-B*57 in that population[57]. A cohort of Irish women infected with contaminated blood products (genotype 1b) had similar protection levels and data showed that specific class II HLA alleles were associated with HCV clearance[58]. Findings of other studies in different populations have shown associations with HLA DQB1*0301 and DRB1*1101, and viral clearance[59]. Although the natural history of HCV infection is believed to be very variable, up to about 20% of chronically infected individuals will develop cirrhosis of the liver over a 20-25-year period, and these people are at increased risk for development of end-stage liver disease and hepatocellular carcinoma [60]. Specific groups are associated with rapid progression of HCV-induced liver fibrosis, including men, people older than age 40 years at time of infection, and individuals who consume 50ml or more of alcohol a day[61], in addition to patients co-infected with HIV [62]. Insulin resistance, obesity, and steatosis can accelerate fibrosis progression in chronic HCV[63]. In fact, insulin resistance has been reported as a specific feature of chronic HCV infection (as compared to chronic hepatitis B) and is associated with genotypes 1 and 4[64]. There is no understanding of the mechanism by which sex affects disease progression; however, an anti-fibrogenic role for oestrogens has been proposed. Menopause was recognized as an independent factor associated with a high stage of fibrosis in a prospective study of 251 women with chronic HCV, and hormone replacement had a protective role[65]. Approximately 3-4 per cent of patients with cirrhosis develop hepatocellular carcinoma per year[66]. Predictions are

that over the next 20-30 years the burden of HCV-associated cancer will rise substantially. This estimate is consistent with recent US data showing an increased prevalence of hepatocellular carcinoma in patients with HCV infection in younger age groups[67]. Several extrahepatic manifestations of HCV infection have been reported, with up to 40-74 per cent of patients developing at least one of these disorders during their illness[68]. In addition to hepatotropism, HCV exhibits particular lymphotropism and this effect could account for many extrahepatic manifestations[69]. The most known and studied syndrome in HCV infection is mixed cryoglobulinemia. Cryoglobulins are immunoglobulins that precipitate below 37 ° C, resulting in systemic vasculitis characterised by the deposition of circulating immune complexes in small and medium sized blood vessels[70]. These molecules are present in up to 50% of HCV-infected patients, although less than 15% have symptomatic disease [71]. An independent association has been described between cryoglobulinaemia and steatosis, and advanced fibrosis[72]. Clinical features of mixed cryoglobulinaemia include cutaneous vasculitis[73], membranous proliferative glomerulonephritis[74], and peripheral neuropathy[75].Treatment is aimed at the underlying virus. Other extrahepatic manifestations include:

- Ø Lympho-proliferative disorders such as lymphoma
- Ø Dermatological problems including porphyria cutanea tarda
- Ø Endocrine disorders such as thyroid dysfunction and diabetes mellitus Various rheumatological syndromes including Sjogren's syndrome and HCV related arthritis [68].

Diagnosis:

A combination of serological and molecular assays (nucleic acid amplification tests) is needed to diagnose HCV infection, guide treatment decisions, and assess response to antiviral treatment. Screening for antibodies against HCV and HCV-RNA testing are techniques used to establish diagnosis of previous or current infection. The HCV genotype determines treatment duration and drug dosage. Molecular assays are also used to define therapeutic response during and at the end of treatment and the sustained virological response (HCV-RNA not detected 6 months after end of treatment)[76]. Patients with suspected acute or chronic HCV infection should be assessed with both an anti-HCV enzyme immunoassay and a sensitive HCV-RNA assay. Acute infection is likely if HCV-RNA is detected without an HCV antibody response which is confirmed by seroconversion days to weeks later and may be delayed or even absent in HIV-infected individuals and other immune-compromised groups[52]. In this setting, acute HCV infection is difficult to distinguish from an acute exacerbation of chronic HCV or from another cause of hepatitis in a patient with chronic HCV, unless an earlier serum sample for HCV testing is available. If neither antibody nor RNA are detectable, acute HCV infection is highly unlikely. The presence of both HCV antibody and RNA in a patient is generally suggestive of chronic HCV infection, particularly in people with signs of chronic liver disease, although these results are also consistent with the recent infection, which can spontaneously clear up [76]. HCV antibody presence and absence of HCV-RNA concord with spontaneous viral clearance or successful treatment. To exclude the possibility of a false-positive antibody result in this situation, alternative serological assays should be used to verify antibody findings.

Anti-HCV drugs:

Before 1989, HCV wasn't identified and it was known as NANB hepatitis. As a trial, acyclovir was used to treat NANB, however it was useless [77]. Then, interferons (IFNs), which were efficiently used to treat hepatitis B, successfully treated NANB hepatitis. Interferons (IFNs) are signaling proteins, which are released normally in the body in response to different pathogens such as viral infection to interfere with the virus replication [78]. The US FDA approved IFN-α as the first anti-HCV drug at 1991, and after HCV identification. However, the use of INFs alone led to relapse and low sustained virological response rate (SVR). Different studies were done to reach the suitable drug combinations, dose and duration of treatment to achieve high SVR. In this review, anti-HCV drugs have been categorized into three groups which discussed as follows:

PEGylated interferon/RBV:

After failure of INFs therapy alone, FDA approved combination of IFN and RBV at 1998. This

combination achieved high SVR (high viral load) rates (34% after 6 months and 42% after 12 months of treatment)[79]. With PEGylation of INF (addition of polyethylene glycol [PEG]) further enhanced virological response was achieved. PEGylated IFN (PEG-INF) has a longer circulation time and a positive SVR rate combined with RBV was higher[80-81]. Accordingly, in 2001, the FDA approved the combination of PEG-IFN and PEG-IFN / RBV and the 6-12 month scheme was considered the standard one until 2011[82]. Despite success of this combination in eradicating the virus, some virus genotypes were not efficiently cured and dependently, led to emergence of new anti-HCV agents such as DAAs (direct acting antiviral agents)[83,84].

Direct acting antivirals (DAAs):

DAAs act directly on the HCV itself, targeting certain steps in its life cycle. Depending on the mechanism of action and viral targets (enzymes or proteins), four classes were developed. Class 1 is NS3/4A protease inhibitors such as glecaprevir, paritaprevir, voxilaprevir and grazoprevir. This class acts via blocking viral protease enzyme, which is responsible for replication. Class 2 is nucleoside and nucleotide nonstructural protein 5B (NS5B) polymerase inhibitors (such as Sofosbuvir). These inhibitors attach to viral RNA, preventing it from replication. Class 3 is nonstructural protein 5A (NS5A) inhibitors. NS5A is a viral protein, which was blocked to prevent the virus from multiplying. Includes ledipasvir, daclatasvir, ombitasvir, pibrentasvir and elbasvir in this class. Last but not least, NS5B polymerase non-nucleoside inhibitors such as dasabuvir are incorporated into HCV which leads to the end of virus reproduction[85]. DAAs should be combined together or with PEG-IFN or RBV in order to enhance the antiviral effect and SVR rates. DAAs dramatically improved treatment of HCV in shorter times and with lower side effects. Therefore, the WHO recommends the wide use of DAAs to enable hepatitis C patients in all the countries from reaching this therapy and living better life. However, the existing limitations of DAAs such as difficult access to this expensive treatment, emergence of viral resistance due to its high mutation rate and risk of developing some adverse effects such as hepatocellular carcinoma, led to evolution of another line of HCV treatment, known as HTAs.

Host targeting antivirals:

HTAs emerged to address DAAs deficiencies. HTAs are considered, reviewed in, to be promising therapy for HCV infections. HTAs act by interfering with the host enzymes and cellular factors required for the HCV life cycle or by improving the host immunity. It could be through host cell entry, replication, or assembly factors that interfere with the virus life cycle[86]. Potent anti-HCV activity with anti-CD81, anti-SRBI monoclonal antibodies, EGFR inhibitor (erlotinib), or NPC1L1 inhibitor (ezetimibe) has been reported to prevent HCV entry[86-89]. One replication inhibitor is microRNA (miRNA), which is non-coding RNA and is used for sequestration of miRNA-122. miRNA-122 is expressed in liver cells and it helps the virus RNA propagation. Additionally, antisense oligonucleotide (miravirsen) specifically targets and inhibits miR-122. Cyclophilin A (CypA) inhibitors (alisporivir/Debio 025, SCY-635 and NIM811) also disrupt the complex of CypA-NS5A, preventing HCV replication and enhancing the host immune response to virus inhibitors[90]. Alpha-glucosidase inhibitors (such as MX-3253) interfere with HCV assembly via misfolding of the virus envelope glycoproteins[91,92]. Due to acting on cellular targets, which is associated with very low mutations, HTAs have higher genetic barriers for resistance.

HCV vaccination:

Global Health Sector Strategy on viral hepatitis (2016-2021) wishes to drastically decrease the new HCV infections by 90% in 2030, which in turn requires affordable access to effective prevention and treatment options all over the world. Despite the ongoing research on treatment of HCV-infected patients, there is still a big demand for vaccination against this virus to avoid the risk of disease transmission between individuals[93,94]. This interprets why there is no available commercial vaccine against HCV, which was identified since 1989. Recent understanding of HCV structure and discovery of some conserved immune system stimulant parts of the virus (such as 5 and 3 UTR) resulted in inspiring possibilities of vaccination against HCV. Therefore, scientists keep seeking a promising vaccine to provide a hope in HCV-free world. Candidates for a promising and affordable HCV vaccine must be able to induce vigorous and prolonged humoral and cellular immune responses to the various genotypes of the virus and prevent the spread of virus among cells[95]. Additionally, preventive vaccine should be able to induce production of nAbs to inhibit the virus from reaching target cells[96]. HCV vaccination could be approached via prophylactic or therapeutic (as an adjunct to HCV antiviral therapy) vaccines. Classical vaccines, which are prepared from whole virus (inactivated or attenuated), are not

recommended with HCV due to biohazard concerns. However, attention has been focused on the use of new vaccination strategies including recombinant proteins (such as recombinant HCV E1 and E2 proteins, recombinant HCV core and NS3-NS4-NS5A-NS5B proteins)[97-98], synthetic peptides[99-100], dendritic cells, virosome-based vaccines and DNA-based vaccines [101] to produce a safe vaccine. These new vaccine approaches are still under clinical trials. Moreover, HCV vaccine could be designed to have multiple epitopes to induce a strong multi-immune response[102-103].

Pharmaceutical Interventions for the Improvement of Anti-HCV Therapy:

Advances in drug delivery systems (DDS) significantly improved the pharmaceutical problems associated with the use of conventional DDS-related antiviral therapy. Advanced DDS involves the lipid polymers composed of particulate carriers. Advanced DDS improved the pharmacokinetic profile and stability of drugs, tissue damage to the sites affected by extravasation and drug targeting (Table 1); Advanced DDS consisting of liposomes and formulations based on lipids are designed to create a more stabilised PEG drug complex by linking PEG to interferons[104]. Classical liposomes also known as 1st generation liposomes exhibit several limitations related to the variability in pharmacokinetics of anti-HCV drugs. Serum proteins affect the drug entrapment in classical liposomes. Incorporation of cholesterol resolved this problem in such a way that it entrapped the drug contents and reduced the leakage of drug. The rapid clearance of drugs from 1st generation liposomes was also problematic. Uptake of these liposomes by mononuclear phagocytes in the liver and spleen results in exacerbation of site specific toxicity and decrease in drug distribution to other tissues. Increasing the half-life of circulating liposomes resolved this issue as mononuclear phagocytes were blocked[105]. Liposomal DDS release triggered allows anti-HCV drugs to reach target sites and improves therapeutic outcomes. There are two types of release triggers for liposomal DDS drugs[106]. Heat, ultrasound and light may act as remote triggers for the release of liposomal DDS, whereas local triggers include enzymes and pH changes. Development of nanoparticles improves drug targeting, increases efficacy and prevents the adverse effects of anti-HCV drugs and the drugs used against HCV induced cancer. The liver, spleen and reticuloendothelial system takes on nanoparticles. Particulate matter with diameters of 100 nm or less is highly accessible to the target site. Nanoparticles with hydrophobicity are absorbed by the liver while those with lipophilia are absorbed by the spleen and reticuloendothelial system[107]. Drugs used against HCV-induced cancer are designed to increase permeability and retention at the target site, inhibit angiogenesis and target the vasculature of tumors [108]. Ribavirin, a nucleoside inhibitor used to treat hepatitis viral genome, is accompanied by accumulation of red blood cells (RBCs) that cause hemolytic anaemia[109-110]. Scientists have therefore designed poly (glycerol-adipate) nanoparticles labelled with rhodamine B isothiocyanate (RBITC-PGA) to target ribavirin specifically to the liver and thereafter to decrease the RBC's take-up rate. These ribavirin nanoparticles could therefore improve HCV therapy by improving the targetability of drug delivery to hepatocytes and endocytic mechanisms[111]. Hyaluronic acid (HA) in combination with gold nanoparticles (AuNPs) has also been found to have a high serum biological activity and chemical stability compared to poly (ethylene glycol) (PEG) nanoparticles[112]. This HA-AuNP nano-complexes was therefore investigated as a delivery vehicle of interferon-α for HCV infection therapy. Seven days after injection of interferon-α encapsulated within HA-AuNP, it was observed that this complex was successfully and specifically delivered to the murine hepatic tissue, while PEG-interferon-α nanoparticles were not observed in the hepatocytes. Finally, it was concluded that the target-specific nano-complex HA-AuNP / interferon-α was effectively useful in the systemic management of HCV infection[112]. On the other hand, hepatic transplantation, the currently available ESLD therapy mainly caused by HCV, has critical obstacles with regard to the shortage of transplantable liver tissue and the discharge of the graft[113]. In one study PEG di-acrylate (PEG-DA)-based nanogel, a non-toxic material, was synthesized to create a platform of three dimensional artificial human liver tissues by entrapment of human progenitor cells in this platform that maintained the hepatic features [114]. This new nanogel platform has exciting consequences for tissue engineering and HCV therapy studies. FDA has approved two recombinant alpha interferons as initial therapy for chronic hepatitis C. It was recommended in 1991 that three million units (MU) of interferon alfa-2b could be given three times per week for a period of 6 months[115]. In 1996, the use of 3 MU of interferon alpha-2a was also approved, three times a week for subcutaneous administration for a 12 month period. Other drugs examined for the treatment of HCV infection included interferon alpha-n1, consensus interferon, interferon derived from leukocytes and several beta interferons. The standardisation and assessment of the comparative biological potency of

Table 1:Pharmaceutical interventions for improving safety and efficacy of anti-HCV drugs.

Problems	Conventional drug delivery system	Advances drug delivery system	Example of intervention	Ref.
Degradation of interferon	Degradation by metabolism, shorter half life, rapid renal clearance, production of antibodies	Pegylation to prevent degradation, immunogenicity and increasing half life	Increase in the stability of Interferon alpha2a through pegylation	116, 117, 118
Poor stability	Reduced incorporation of hydrophobic drug in aqueous medium	Liposomes provide the hydrophilic and hydrophobic environment for incorporation of drugs	Increase in the stability of interferon with liposomes followed by pegylation	119
Tissue damages on extravasation of drugs	Inadvertent extravasations of toxic drugs causes tissue damages	Advanced DDS reduces the tissue damages by extravasation due to slow drug release	Formulation of ribavirin containing liposomes to prevent hemolysis	120
Poor biodistribution	The drug widely distributes so that it causes damage to unrelated tissues	In controlled release DDS, the drug releases slowly so that volume of drug distribution is lowered which reduces side effects	Biodegradable microspheres of interferons to increase the efficacy and dose related adverse effects	121
Rapid clearance	Rapid clearance of drugs through kidney necessitates administration of high dose or continuous infusion	In advanced DDS, the clearance of the drug is decreased altering the pharmacokinetics of drug	Pegylation, attachment of dextran or crosslinking of proteins decreases clearance of interferon	122
Lack of target tissue selectivity	The drug is widely distributed so that the concentrationof drug is low at the target site resulting in reduced therapeutic effect	In advanced DDS, the concentration of the drug is high at the target site	Increased liver targeting of ribavirin with niosomes. Nanoparticle formulations of ribavirin can be used for viral infections in the brain. Surface of nano-carriers is modified so as to increase the delivery of ritonavir to cells	123, 124

different interferons remains problematic, however.

Conclusion & future perspective of nanomedicine-based HCV therapy:

Like any serious viral infections, HCV is a global issue of concern, which affects millions of people with negative effects on health and socioeconomic development. Since the discovery of HCV in 1989, there is an emergence of a huge number of new treatments, promising HCV patients a better life. With the ability to combine and integrate tools, nanotechnology offers a powerful contribution to the future of HCV prevention, diagnosis and treatment through imparting unique features to the drugs. These unique features include surface functionalization with one or more targeting ligands, imparting high specificity and affinity to liver cells and consequently off-target accumulation, which results in very low side effects[125]. On the other hand, the ability of nanosystems to house more than one therapeutic moiety could result in multivalent drug therapy with controlled release behavior. Additionally, HCV gene therapy, such as using siRNA, would not be successful without a nanocarrier, which is able to efficiently condensate and deliver intact genetic materials to their targets, affecting the virus life cycle. Nanomedicine, which is able to protect and control fate of the encapsulated drug, has enormous abilities to draw a clear future of HCV therapy through overcoming several challenges. Some of these challenges include viral resistance, patient access to effective treatment, shortening the duration of treatment and availability of prophylactic vaccines to prevent further spread of HCV. Emergence of HCV resistance remains for the moment as a major challenge to overcome. Due to its low genetic barrier to resistance[126], which requires

the search for new treatment regimens, effective DAAs monotherapy could be hindered. Nanosystems, however, which have the ability to house more than one therapeutic moiety, could easily deliver different combination therapies for HCV, reducing the risk of failure in the treatment[127]. On the other hand, HTAs have a higher genetic barrier to resistance than DAAs, based on the mechanism of action. Many of these HTAs are genetic materials, which need promising nanocarriers to be efficiently delivered to their targets, overcoming DAA shortcomings. Parallel to development of effective anti-HCV therapy, global elimination of the virus depends also on reducing the cost of these treatment and improving the patient's access to these drugs. The proposed nanosystems are anticipated to reduce the encapsulated dose while keeping on sufficient drug efficacy [128]. Reducing the dose of expensive drugs will result in reduction of the total production cost and consequently, treatment will be extended to all HCV patients. The current 6-week therapy is of long duration, and shortening to four weeks or less appears to be a challenge to improve patient compliance[129]. Encapsulation of anti-HCV agents within surface-modified and functionalized nanosystems results in optimised dosing of the drug and increased delivery to the target site. Surface functionalization with certain targeting moieties has the ability to direct anti-HCV containing nanosystem toward liver cells, where the virus mainly multiplies. It is believed that with engineered nanosystems bearing moieties to target its delivery, there is a hope to shorten treatment duration for all HCV populations. Many HCV patients are unaware of their infection and are considered as a main reservoir for infection especially among young persons who inject drugs. Using nanotechnology, a prophylactic vaccine, which was not available till now and is considered a necessity to prevent further spread of the virus globally, could be approached.

REFERENCES:

1. Sherlock, S. (1996) Digest. Dis. Sci. 41, 3S–5S.
2. Houghten, M. (1996) in Fields Virology (3rd edn) (Fields, B.N. et al., eds), pp. 1035–1058, Raven Press.
3. Q.L. Choo, G. Kuo, A.J. Weiner, L.R. Overby, D.W. Bradley, M. Houghton, Isolation of a cDNAS clone derived from a blood non-A, non-B viral hepatitis genome, Science 244 (1989) 359e362.
4. M. Maeno, K. Maminaka, H. Sugimoto, M. Esumi, N. Hayashi, K. Komatsu, K. Abe, S. Sekiguchi, M. Yano, K. Mizuno, A cDNA clone closely associated with non-A, non-B hepatitis, Nucleic Acids Res. 18 (1990) 2685e2689.
5. World Health Organization. Hepatitis C fact sheet. Available from: URL: http://www.who.int/mediacentre/factsheets/fs164/en. Updated April 2014. Accessed February 18, 2015.
6. Mohd Hanafiah K, Groeger J, Flaxman AD, Wiersma ST. Global epidemiology of hepatitis C virus infection: new estimates of agespecific antibody to HCV seroprevalence. Hepatology 2013; 57: 1333-1342.
7. Hauri AM, Armstrong GL, Hutin YJ. The global burden of disease attributable to contaminated injections given in health care settings. Int J STD AIDS 2004; 15: 7-16.
8. Alberti A. What are the comorbidities influencing the management of patients and the response to therapy in chronic hepatitis C? Liver Int 2009; 29 Suppl 1: 15-18.
9. Ponziani FR, Gasbarrini A, Pompili M, Burra P, Fagiuoli S. Management of hepatitis C virus infection recurrence after liver transplantation: an overview. Transplant Proc 2011; 43: 291-295.
10. Davis GL, Alter MJ, El-Serag H, Poynard T, Jennings LW. Aging of hepatitis C virus (HCV)-infected persons in the United States: a multiple cohort model of HCV prevalence and disease progression. Gastroenterology 2010; 138: 513-521, 521.e1-521.e6.
11. Razavi H, Waked I, Sarrazin C, Myers RP, Idilman R, Calinas F, Vogel W, Mendes Correa MC, et al. The present and future disease burden of hepatitis C virus (HCV) infection with today's treatment paradigm. J Viral Hepat 2014; 21 Suppl 1: 34-59.
12. Kanwal F, Hoang T, Kramer JR, Asch SM, Goetz MB, Zeringue A, Richardson P, El-Serag HB. Increasing prevalence of HCC and cirrhosis in patients with chronic hepatitis C virus infection. Gastroenterology 2011; 140: 1182-1188.e1.
13. Arase Y, Suzuki F, Suzuki Y, Akuta N, Kobayashi M, Kawamura Y, Yatsuji H, Sezaki H, Hosaka T, Hirakawa M, Ikeda K, Kumada H. Sustained virological response reduces incidence of onset of type 2 diabetes in chronic hepatitis C. Hepatology 2009; 49: 739-744.
14. Centers for Disease Control. Disease burden from viral hepatitis A, B, and C in the United States. Available from: URL: http:// www.cdc.gov/hepatitis/Statistics/index.htm.
15. Centers for Disease Control and Prevention. CDC Health Information for International Travel 2014. New York:

Oxford University Press, 2014. Available from: URL: http://wwwnc.cdc. Gov/travel /yellowbook /2014 /chapter-3-infectious-diseases-relatedto-travel/hepatitis-c.

16. Shepard CW, Finelli L, Alter MJ. Global epidemiology of hepatitis C virus infection. Lancet Infect Dis 2005; 5: 558-567.
17. Mohamoud YA, Mumtaz GR, Riome S, Miller D, Abu-Raddad LJ. The epidemiology of hepatitis C virus in Egypt: a systematic review and data synthesis. BMC Infect Dis 2013; 13: 288.
18. Halliday J, Klenerman P, Barnes E. Vaccination for hepatitis C virus: closing in on an evasive target. Expert Rev Vaccines 2011; 10: 659–72.
19. Kapoor A, Simmonds P, Gerold G, et al. Characterization of a canine homolog of hepatitis C virus. Proc Natl Acad Sci USA 2011; 108: 11608–13.
20. Lyons S, Kapoor A, Sharp C, et al. Nonprimate hepaciviruses in domestic horses, United kingdom. Emerg Infect Dis 2012; 18: 1976–82.
21. Kapoor A, Simmonds P, Scheel TK, et al. Identifi cation of rodent homologs of hepatitis C virus and pegiviruses. MBio 2013; 4: e00216–13.
22. Pybus OG, Barnes E, Taggart R, et al. Genetic history of hepatitis C virus in East Asia. J Virol 2009; 83: 1071–82.
23. Simmonds P. Genetic diversity and evolution of hepatitis C virus—15 years on. J Gen Virol 2004; 85: 3173–88.
24. Pybus OG, Charleston MA, Gupta S, Rambaut A, Holmes EC, Harvey PH. The epidemic behavior of the hepatitis C virus. Science 2001; 292: 2323–25.
25. Gray RR, Salemi M, Klenerman P, Pybus OG. A new evolutionary model for hepatitis C virus chronic infection. PLoS Pathog 2012; 8: e1002656.
26. Wakita T, Pietschmann T, Kato T, et al. Production of infectious hepatitis C virus in tissue culture from a cloned viral genome. Nat Med 2005; 11: 791–96.
27. Meredith LW, Wilson GK, Fletcher NF, McKeating JA. Hepatitis C virus entry: beyond receptors. Rev Med Virol 2012; 22: 182–93.
28. Shulla A, Randall G. Hepatitis C virus–host interactions, replication, and viral assembly. Curr OpinVirol 2012; 2: 725–32.
29. Catanese MT, Uryu K, Kopp M, et al. Ultrastructural analysis of hepatitis C virus particles. Proc Natl Acad Sci USA 2013; 110: 9505–10.
30. Kim JL, Morgenstern KA, Lin C, et al. Crystal structure of the hepatitis C virus NS3 protease domain complexed with a synthetic NS4A cofactor peptide. Cell 1996; 87: 343–55.
31. Love RA, Parge HE, Wickersham JA, et al. The crystal structure of hepatitis C virus NS3 proteinase reveals a trypsin-like fold and a structural zinc binding site. Cell 1996; 87: 331–42.
32. Lesburg CA, Cable MB, Ferrari E, Hong Z, Mannarino AF, Weber PC. Crystal structure of the RNA-dependent RNA polymerase from hepatitis C virus reveals a fully encircled active site. Nat Struct Biol 1999; 6: 937–43.
33. Duggal P, Thio CL, Wojcik GL, et al. Genome-wide association study of spontaneous resolution of hepatitis C virus infection: data from multiple cohorts. Ann Intern Med 2013; 158: 235–45.
34. Prokunina-Olsson L, Muchmore B, Tang W, et al. A variant upstream of IFNL3 (IL28B) creating a new interferon gene IFNL4 is associated with impaired clearance of hepatitis C virus. Nat Genet 2013; 45: 164–71.
35. Khakoo SI, Thio CL, Martin MP, et al. HLA and NK cell inhibitory receptor genes in resolving hepatitis C virus infection. Science 2004; 305: 872–74.
36. Fitzmaurice K, Petrovic D, Ramamurthy N, et al. Molecular footprints reveal the impact of the protective HLA-A*03 allele in hepatitis C virus infection. Gut 2011; 60: 1563–71.
37. Shoukry NH, Grakoui A, Houghton M, et al. Memory CD8+ T cells are required for protection from persistent hepatitis C virus infection. J Exp Med 2003; 197: 1645–55.
38. Barnes E, Folgori A, Capone S, et al. Novel adenovirus-based vaccines induce broad and sustained T cell responses to HCV in man. Sci Transl Med 2012; 4: 115ra1.
39. Wahid A, Dubuisson J. Virus-neutralizing antibodies to hepatitis C virus. J Viral Hepat 2013; 20: 369–76.
40. Giang E, Dorner M, Prentoe JC, et al. Human broadly neutralizing antibodies to the envelope glycoprotein complex of hepatitis C virus. Proc Natl Acad Sci USA 2012; 109: 6205–10.
41. Kong L, Giang E, Nieusma T, et al. Structure of hepatitis C virus envelope glycoprotein E2 antigenic site 412 to 423 in complex with antibody AP33. J Virol 2012; 86: 13085–88.
42. Alter MJ. Epidemiology of hepatitis C virus infection. World J Gastroenterol 2007; 13: 2436–41.
43. Roberts EA, Yeung L. Maternal-infant transmission of

hepatitis C virus infection. Hepatology 2002; 36 (5 suppl 1): S106–13.
44. Terrault NA. Sexual activity as a risk factor for hepatitis C. Hepatology 2002; 36 (5 suppl 1): S99–105.
45. Busch MP, Glynn SA, Stramer SL, et al. A new strategy for estimating risks of transfusion-transmitted viral infections based on rates of detection of recently infected donors. Transfusion 2005; 45: 254–64.
46. Thorpe LE, Ouellet LJ, Hershow R, et al. Risk of hepatitis C virus infection among young adult injection drug users who share injection equipment. Am J Epidemiol 2002; 155: 645–53.
47. Jain S, Goharkhay N, Saade G, Hankins GD, Anderson GD. Hepatitis C in pregnancy. Am J Perinatol 2007; 24: 251–56.
48. McIntyre PG, Tosh K, McGuire W. Caesarean section versus vaginal delivery for preventing mother to infant hepatitis C virus transmission. Cochrane Database Syst Rev 2006; 4: Cd005546.
49. Rooney G, Gilson RJ. Sexual transmission of hepatitis C virus infection. Sex Transm Infect 1998; 74: 399–404.
50. Danta M, Brown D, Bhagani S, et al. Recent epidemic of acute hepatitis C virus in HIV-positive men who have sex with men linked to high-risk sexual behaviours. AIDS 2007; 21: 983–91.
51. Alter MJ. Epidemiology of viral hepatitis and HIV co-infection. J Hepatol 2006; 44 (1 suppl): S6–9.
52. Klenerman P, Kim A. HCV-HIV coinfection: simple messages from a complex disease. PLoS Med 2007; 4: e240.
53. Daar ES, Lynn H, Donfi eld S, et al. Relation between HIV-1 and hepatitis C viral load in patients with hemophilia. J Acquir Immune Defi c Syndr 2001; 26: 466–72.
54. Bica I, McGovern B, Dhar R, et al. Increasing mortality due to endstage liver disease in patients with human immunodefi ciency virus infection. Clin Infect Dis 2001; 32: 492–97.
55. Grebely J, Matthews GV, Dore GJ. Treatment of acute HCV infection. Nature Rev Gastroenterol Hepatol. 2011; 8:265-74.
56. Hoofnagle JH. Course and outcome of hepatitis C. Hepatology 2002; 36 (5 suppl 1): S21–29.
57. Chuang WC, Sarkodie F, Brown CJ, et al. Protective eff ect of HLAB57 on HCV genotype 2 infection in a West African population. J Med Virol 2007; 79: 724–33.
58. Fanning LJ. The Irish paradigm on the natural progression of hepatitis C virus infection: an investigation in a homogeneous patient population infected with HCV 1b. Int J Mol Med 2002; 9: 179–84.
59. Asselah T, Bieche I, Paradis V, Bedossa P, Vidaud M, Marcellin P. Genetics, genomics, and proteomics: implications for the diagnosis and the treatment of chronic hepatitis C. Semin Liver Dis 2007; 27: 13–27.
60. Rustgi VK. The epidemiology of hepatitis C infection in the United States. J Gastroenterol 2007; 42: 513–21.
61. Poynard T, Yuen MF, Ratziu V, Lai CL. Viral hepatitis C. Lancet 2003; 362: 2095–100.
62. Monga HK, Rodriguez-Barradas MC, Breaux K, et al. Hepatitis C virus infection-related morbidity and mortality among patients with human immunodefi ciency virus infection. Clin Infect Dis 2001; 33: 240–47.
63. Asselah T, Rubbia-Brandt L, Marcellin P, Negro F. Steatosis in chronic hepatitis C: why does it really matter? Gut 2006; 55: 123–30.
64. Moucari R, Asselah T, Cazals-Hatem D, et al. Insulin resistance in chronic hepatitis C: association with genotypes 1 and 4, serum HCV RNA level, and liver fi brosis. Gastroenterology 2008; 134: 416–23.
65. Codes L, Asselah T, Cazals-Hatem D, et al. Liver fi brosis in women with chronic hepatitis C: evidence for the negative role of the menopause and steatosis and the potential benefi t of hormone replacement therapy. Gut 2007; 56: 390–95.
66. Davis GL, Albright JE, Cook SF, Rosenberg DM. Projecting future complications of chronic hepatitis C in the United States. Liver Transpl 2003; 9: 331–38.
67. El-Serag HB, Mason AC. Rising incidence of hepatocellular carcinoma in the United States. N Engl J Med 1999; 340: 745–50.
68. Galossi A, Guarisco R, Bellis L, Puoti C. Extrahepatic manifestations of chronic HCV infection. J Gastrointestin Liver Dis 2007; 16: 65–73.
69. Agnello V, De Rosa FG. Extrahepatic disease manifestations of HCV infection: some current issues. J Hepatol 2004; 40: 341–52.
70. Misiani R, Bellavita P, Fenili D, et al. Hepatitis C virus infection in patients with essential mixed cryoglobulinemia. Ann Intern Med 1992; 117: 573–77.
71. Pawlotsky JM, Roudot-Thoraval F, Simmonds P, et al. Extrahepatic immunologic manifestations in chronic hepatitis C and hepatitis C virus serotypes. Ann Intern Med 1995; 122: 169–73.
72. Saadoun D, Asselah T, Resche-Rigon M, et al.

Cryoglobulinemia is associated with steatosis and fi brosis in chronic hepatitis C. Hepatology 2006; 43: 1337–45.

73. Sansonno D, Cornacchiulo V, Iacobelli AR, Di Stefano R, Lospalluti M, Dammacco F. Localization of hepatitis C virus antigens in liver and skin tissues of chronic hepatitis C virus-infected patients with mixed cryoglobulinemia. Hepatology 1995; 21: 305–12.
74. Johnson RJ, Gretch DR, Yamabe H, et al. Membranoproliferative glomerulonephritis associated with hepatitis C virus infection. N Engl J Med 1993; 328: 465–70.
75. Ferri C, La Civita L, Cirafi si C, et al. Peripheral neuropathy in mixed cryoglobulinemia: clinical and electrophysiologic investigations. J Rheumatol 1992; 19: 889–95.
76. Chevaliez S, Pawlotsky JM. Hepatitis C virus: virology, diagnosis and management of antiviral therapy. World J Gastroenterol 2007; 13: 2461–66.
77. Pappas SC, Hoofnagle JH, Young N, Straus SE, Jones EA. Treatment of chronic non-A, non-B hepatitis with acyclovir: pilot study. J. Med. Virol. 15(1), 1–9 (1985).
78. Marie MA, John J, Krishnappa LG, Gopalkrishnan S, Bindurani SR. Role of interleukin-6, gamma interferon and adenosinedeaminase markers in management of pleural effusion patients.West Indian Med. J. 62 (9), 803–807 (2013).
79. Poynard T, Marcellin P, Lee SS et al. Randomised trial of interferon α2b plus ribavirin for 48 weeks or for 24 weeks versus interferon α2b plus placebo for 48 weeks for treatment of chronic infection with hepatitis C virus. Lancet 352(9138), 1426–1432 (1998).
80. Lindsay KL, Trepo C, Heintges T et al. A randomized, double-blind trial comparing pegylated interferon alfa-2b to interferon alfa-2b as initial treatment for chronic hepatitis C. Hepatology 34(2), 395–403 (2001).
81. Reddy KR, Wright TL, Pockros PJ et al. Efficacy and safety of pegylated (40-kd) interferon α-2a compared with interferon α-2a in noncirrhotic patients with chronic hepatitis C. Hepatology 33(2), 433–438 (2001).
82. Mcewan P, Ward T, Webster S, Kalsekar A, Brenner M, Yuan Y. Modeling the cost–effectiveness of the all oral, direct-acting antiviral regimen daclatasvir plus sofosbuvir in patients co-infected with hepatitis C virus (HCV) and HIV. Value Health 18(7), A628 (2015).
82. Poenisch M, Bartenschlager R. New insights into structure and replication of the hepatitis C virus and clinical implications. Semin. Liver Dis. 30(4), 333–347 (2010).
84. Pawlotsky JM. Therapy: avoiding treatment failures associated with HCV resistance. Nat. Rev. Gastroenterol. Hepatol. 12(12), 673 (2015).
85. Poordad F, Dieterich D. Treating hepatitis C: current standard of care and emerging direct-acting antiviral agents. J. Viral Hepat. 19(7), 449–464 (2012).
86. Zeisel MB, Lupberger J, Fofana I, Baumert TF. Host-targeting agents for prevention and treatment of chronic hepatitis C – perspectives and challenges. J. Hepatol. 58(2), 375–384 (2013).
87. Meuleman P, Hesselgesser J, Paulson M et al. Anti-CD81 antibodies can prevent a hepatitis C virus infection in vivo. Hepatology 48(6), 1761–1768 (2008).
88. Meuleman P, Catanese MT, Verhoye L et al. A human monoclonal antibody targeting scavenger receptor class B type I precludes hepatitis C virus infection and viral spread in vitro and in vivo. Hepatology 55(2), 364–372 (2012).
89. Lacek K, Vercauteren K, Grzyb K et al. Novel human SR-BI antibodies prevent infection and dissemination of HCV in vitro and in humanized mice. J. Hepatol. 57(1), 17–23 (2012).
90. Tajima A. DAA (direct-acting antivirals) and HATs (host-targeting antivirals) in 2014. JSM Gastroenterol. Hepatol. 2(2), 1016 (2014).
91. Chapel C, Garcia C, Roingeard P et al. Antiviral effect of α-glucosidase inhibitors on viral morphogenesis and binding properties of hepatitis C virus-like particles. J. Gen. Virol. 87(4), 861–871 (2006).
92. Chapel C, Garcia C, Bartosch B et al. Reduction of the infectivity of hepatitis C virus pseudoparticles by incorporation of misfolded glycoproteins induced by glucosidase inhibitors. J. Gen. Virol. 88(4), 1133–1143 (2007).
93. Jawaid A, Khuwaja AK. Treatment and vaccination for hepatitis C: present and future. J. Ayub Med. Coll. Abbottabad 20(1), 129–133 (2008).
94. Duffy S, Shackelton LA, Holmes EC. Rates of evolutionary change in viruses: patterns and determinants. Nat. Rev. Genet. 9(4), 267 (2008).
95. Ippolito G, Capobianchi MR, Lanini S, Antonelli G. Is hepatitis C virus eradication around the corner only 25 years after its discovery? Int. J. Antimicrob. Agents 45(2), 111–112 (2015).
96. Burton DR, Poignard P, Stanfield RL, Wilson IA.

Broadly neutralizing antibodies present new prospects to counter highly antigenically diverse viruses. Science 337(6091), 183–186 (2012).
97. Choo Q, Kuo G, Ralston R et al. Vaccination of chimpanzees against infection by the hepatitis C virus. Proc. Natl. Acad. Sci. USA 91(4), 1294–1298 (1994).
98. Polakos NK, Drane D, Cox J et al. Characterization of hepatitis C virus core-specific immune responses primed in rhesus macaques by a nonclassical ISCOM vaccine. J. Immunol. 166(5), 3589–3598 (2001).
99. Klade CS, Wedemeyer H, Berg T et al. Therapeutic vaccination of chronic hepatitis C nonresponder patients with the peptide vaccine IC41. Gastroenterology 134(5), 1385–1395, e1381 (2008).
100. Wedemeyer H, Schuller E, Schlaphoff V et al. Therapeutic vaccine IC41 as late add-on to standard treatment in patients with chronic hepatitis C. Vaccine 27(37), 5142–5151 (2009).
101. Puig M, Mihalik K, Tilton JC et al. CD4+ immune escape and subsequent T-cell failure following chimpanzee immunization against hepatitis C virus. Hepatology 44(3), 736–745 (2006).
102. Chattergoon M, Boyer J, Weiner DB. Genetic immunization: a new era in vaccines and immune therapeutics. FASEB J. 11(10), 753–763 (1997).
103. Zeng R, Li G, Ling S et al. A novel combined vaccine candidate containing epitopes of HCV NS3, core and E1 proteins induces multi-specific immune responses in BALB/c mice. Antiviral Res. 84(1), 23–30 (2009).
104. Allen TM, Cullis PR. Drug delivery systems: entering the mainstream. Science. 2004;303:1818-22.
105. Kumari A, Yadav SK, Yadav SC. Biodegradable polymeric nanoparticles based drug delivery systems. Colloids Surf B Biointerfaces. 2010;75:1-18.
106. Allen TM, Cullis PR. Liposomal drug delivery systems: From concept to clinical applications. Adv Drug Delivery Rev. 2013;65:36-48.
107. Zhou K, Wang Y, Huang X, Luby-Phelps K, Sumer BD, Gao J. Tunable, ultrasensitive pH-responsive nanoparticles targeting specific endocytic organelles in living cells. Angew Chem. 2011;123:6233-8.
108. Brannon-Peppas L, Blanchette JO. Nanoparticle and targeted systems for cancer therapy. Adv Drug Delivery Rev. 2012;64:206-12.
109. Schekman, R., & Singer, S. J. (1976). Clustering and endocytosis of membrane receptors 1050 can be induced in mature erythrocytes of neonatal but not adult humans. Proc Natl 1051 Acad Sci U S A 73, 4075–4079.
110. Rothen-Rutishauser, B. M., Schürch, S., Haenni, B., Kapp, N., & Gehr, P. (2006). Interaction 1047 of fine particles and nanoparticles with red blood cells visualized with advanced mi- 1048 croscopic techniques. Environ Sci Tech 40, 4353–4359.
111. Abo-zeid, Y., Irving, W., Thomson, B., & Garnett, M. (2013). Nanoparticle delivery systems 819 for HCV treatment: do nanoparticles avoid uptake by erythrocytes? Viral Hepatitis 820 Congress 2013 September 26–28, 2013; Frankfurt, Germany.
112. Lee, M. -Y., Yang, J. -A., Jung, H. S., Beack, S., Choi, J. E., Hur, W., et al. (2012). Hyaluronic acid-gold nanoparticle/interferon α complex for targeted treatment of hepatitis C virus infection. ACS Nano 6, 9522–9531.
113. Alter, M. J., Kruszon-Moran, D., Nainan, O. V., McQuillan, G. M., Gao, F., Moyer, L. A., et al. 822 (1999). The prevalence of hepatitis C virus infection in the United States, 1988 823 through 1994. N Engl J Med 341, 556–562.
114. Hubbell, J. A. (2004). Tissue and cell engineering. Curr Opin Biotechnol 15, 381–382.
115. McHutchison JG, Lawitz EJ, Shiffman ML, Muir AJ, Galler GW, McCone J, et al. Peginterferon alfa-2b or alfa-2a with ribavirin for treatment of hepatitis C infection. New Engl J Med. 2009; 361:580-93.
116. Liu Y, Goff, RD, Zhou D, Mattner J, Sullivan BA, Khurana A, et al. A modified α-galactosyl ceramide for staining and stimulating natural killer T cells. J Immunol Meth. 2006; 312:34-9.
117. Harris JM, Chess RB. Effect of pegylation on pharmaceuticals. Nature Rev Drug Discov. 2003; 2:214-21.
118. Veronese FM, Pasut G. PEGylation, successful approach to drug delivery. Drug Discov Today. 2005; 10:1451-8.
119. Milla P, Dosio F, Cattel L. PEGylation of proteins and liposomes: a powerful and flexible strategy to improve the drug delivery. Curr Drug Metab. 2012; 13:105-19.
120. Guo H, Sun S, Yang Z, Tang X, Wang Y. Strategies for ribavirin prodrugs and delivery systems for reducing the side-effect hemolysis and enhancing their therapeutic effect. J Control Release. 2015;209:27-36.
121. Sánchez A, Tobío M, González L, Fabra A, Alonso MJ. Biodegradable micro-and nanoparticles as longterm delivery vehicles for interferon-alpha. Eur J Pharm Sci.

delivery vehicles for interferon-alpha. Eur J Pharm Sci. 2003; 18:221-9.

122. Sheffield W. Modification of clearance of therapeutic and potentially therapeutic proteins. Curr Drug Targets Cardiovasc Hematol Disord. 2001;1:1-22.

123. Hashim F, El-Ridy M, Nasr M, Abdallah Y. Preparation and characterization of niosomes containing ribavirin for liver targeting. Drug Deliv. 2010;17:282-7.

124. Gaillard PJ, Visser CC, de Boer M, Appeldoorn CC, Rip J. Blood-to-brain drug delivery using nanocarriers. In: Hammarlund-Udenaes M, de Lange ECM, Thorne RG (eds): Drug delivery to the brain: physiological concepts, methodologies and approaches (pp 433-54). New York: Springer, 2014 (AAPS Advances in the Pharmaceutical Sciences Series, Vol. 10).

125. Noura H Abd Ella, Hesham M Tawfeek, James John, Helal F Hetta. Nanomedicine as a future therapeutic approach for Hepatitis C virus. Nanomedicine (2019) 14(11), 1471–1491

126. Mccown MF, Rajyaguru S, Le Pogam S et al. The hepatitis C virus replicon presents a higher barrier to resistance to nucleoside analogs than to nonnucleoside polymerase or protease inhibitors. Antimicrob. Agents Chemother. 52(5), 1604–1612 (2008).

127. Lee SH, Moon JS, Pak BY et al. HA1077 displays synergistic activity with daclatasvir against hepatitis C virus and suppresses the emergence of NS5A resistance-associated substitutions in mice. Sci. Rep. 8(1), 12469 (2018).

128. Ventola CL. Progress in nanomedicine: approved and investigational nanodrugs. Pharm. Ther. 42(12), 742–755 (2017).

129. Deterding K, Spinner C, Schott E et al. Six weeks of sofosbuvir/ledipasvir (SOF/LDV) are sufficient to treat acute hepatitis C virus genotype 1 monoinfection: the HEPNET acute HCV IV study. J. Hepatol. 64(2), S211 (2016).

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Evaluation of Efficacy of DAB for Phi Bodies in Acute Leukemia

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Original Research Article

ABSTRACT

Diagnosing the type and sub-type of Leukemia is very important as the therapy, prognosis and survival rate changes with each type and sub-type. In the present study French American British (FAB) morphologic classification is used and 60 cases of Leukemia were evaluated by studying the detailed clinical features, morphology on peripheral blood smear and bone marrow aspiration. Out of the 60 cases we found that 40 cases were of acute Leukemia and 20 cases of chronic Leukemia. Out of which 24 were of acute Myeloid Leukemia, 16 of acute Lymphoid Leukemia. There were 15 cases of CML and 5 cases of CLL. Phi bodies appear to be characteristics of immature Myeloid cells in Leukemia and are seen with a higher frequency than Auer rods in acute Myeloid Leukemia

KEY WORDS: Phi bodies, Leukemia, DAB

INTRODUCTION:

Leukemia is a neoplastic proliferation of hematopoietic cells and forms a major proportion of hematopoietic neoplasm that are diagnosed worldwide. Leukemia is classified into two broad groups, Myeloid and Lymphoid, based on the origin of the leukemic stem cell clone[1]. Diagnosing the type and sub-type of Leukemia is very important as the therapy, prognosis and survival rate changes with each type and sub-type. Although the French American British (FAB) morphologic classification of Myeloid and Lymphoid neoplasm has been used since many years, the discovery of number of genetic lesions that predict the clinical behavior and outcome better than morphology alone. It necessitates the incorporation of specific genetic data in the classification scheme[1]. The diagnosis of acute Leukemia entails a stepwise approach. First in the sequence and of importance is the distinction of acute Leukemia from other neoplastic diseases and reactive disorders. Second is differentiating acute Myeloid (AML) from acute lymphoblastic (ALL) Leukemia. The third facet is the classification of AML and ALL into categories that define treatment and prognostic groups. In most cases, the first two facets of diagnosis of acute Leukemia can be achieved by careful morphological assessment of blood and bone marrow smears and marrow trephine biopsy sections[2]. By assessing the morphologic features together, a majority of cases of AML and ALL can be accurately diagnosed. In some cases of poorly differentiated acute Leukemia, however, the morphologic features may be equivocal, requiring additional studies [3].

The present study was conducted to assess the cytochemical reaction for Myeloperoxidase as a valuable tool in the classification of acute Leukemia, chiefly in the distinction between acute Myeloid and acute lymphoblastic leukaemia[4]. Auer rods[5] are usually visible with Romanovsky stains in blast cells from various acute Myeloid types, particularly those with myeloblastic-promyelocytic differentiation (Ml to M3 of the FAB classification).'They have been considered to result from aberrations of the primary (azurophil) granules of early granulocytic cells[6] and are often seen more easily in peroxidase preparations. Hanker et al[7], described a new type of rod, the Phi body, not visualized with Romanovsky dyes but only by means of a peroxidase reaction using 3,3'diaminobenzidine (DAB), and recommended that they were also characteristic of acute Myeloid Leukemia. We have investigated the presence of Auer rods and Phi bodies in patients with acute Leukemia in order to clarify the relation of Auer rods to the so-called Phi bodies[8].

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AIMS & OBJECTIVES:

1. To classify Leukemia and subtype acute Leukemia with the help of Cytochemistry according to French American British (FAB) Classification.
2. To study the Routine MPO with Benzedine Hydrochloride and DAB in Acute Leukemia and its sub types [3,8].
3. To Demonstrate the Phi bodies in AML blast only when DAB is used[9].

MATERIALS & METHODS:

The hematological laboratory based study spanned over a period of 2 years. The peripheral blood smears & bone marrow aspirates of all morphologically diagnosed Acute Leukemia cases received in the Department of Pathology NKP SIMS LMH Nagpur were studied.

INCLUSION CRITERIA:

Patients of all age groups who presented with clinical features and abnormal hematological findings suggestive of Leukemia (Peripheral Smear and Bone marrow aspiration smear).

EXCLUSION CRITERIA:

Patient with other hematological malignancies like lymphomas and multiple myelomas were excluded.

The relevant clinical history was obtained in each case, routine blood counts performed and peripheral smear and bone marrow aspirates studied in detail. Smears were stained with standard Romanovsky stains (Lieshman stain) and studied for morphology of cells. Hematological investigations were done on a 5 part cell counter. Cytochemical stains such as Myeloperoxidase, Non specific esterase; Sudan Black B and Periodic acid Schiff were done wherever needed for typing acute Leukemia cases. Kits manufactured by FAR SRL from Verona Italy were used for Cytochemistry[3].Leukemia was classified according to the FAB criteria[1] using May-Grunewald-Giemsa stain : Sudan Black B,naphthol-AS acetate esterase ± NaF, a-naphthyl acetate esterase ± NaF, acid phosphatase, and lysozyme.The Myeloperoxidase reaction was observed on peripheral blood smear from all acute Leukemia (24 Myeloid and 16 lymphoblastic) cases with the following reagents for comparative study:

(1) Benzedine dihydrochloride and (2) 3,3'diaminobenzidine tetra hydrochloride (DAB), introduced by Graham and Karnovsky in 1966.[10] Substrates (1) used according to previous techniques.[11]

(2) DAB was tested according to the simplified technique of Hanker et al.[12] with minor modifications, as follows:

FIXATION:

Smears were fixed for One minute in a mixture of 1.25% glutaraldehyde and 1% formaldehyde in 0.1 M phosphate buffer (pH 7.3); rinsing in 0.9% NaCI.

INCUBATION:

Smears were immersed One minute in a medium (prepared just before use) containing 5 mg DAB, 10 ml Tris HCI buffer (0.05 M, pH 7.6), and 0.1 ml 1% H_2O_2. Slides are then rinsed briefly in Tris-HCI buffer and immersed for 1 minute in 0.5% CuSO4 in Tris-HCl buffer and rinsed again in 0.9% NaCl.

COUNTERSTAIN:

Ten minutes in a 10% solution of Giemsa, than dry & mounted in DPX [8].

thoroughly mixed in a vacuum mixing unit (WHIPMIX) for 30 seconds as suggested by the manufacturer. After 45 minutes the casting ring was placed in cool burnout furnace (HIHEAT- LABO-31 CONFIDENT) for 60 minutes, the highest temperature programmed was 950°C. The ring was allowed to stand for another 10 min. to ensure complete wax burn out. After burnout the casting ring was carefully placed in casting machine and casting was done as per manufactures' instructions

The casting ring was allowed to bench cool to room temperature and then the casting was divested from the refractory. The sprues were detached using high speed cut-off discs and any adherent investment removed by sand blasting.

For standardization of specimens the castings were cleaned with 250 micron alumina particle (BEGO). Each Specimen was sand blasted for 5 min from distance of 50 mm. in the sandblaster.

The samples were first subjected for surface roughness test and later for tensile strength test. This order was followed as the test specimen became distorted once they are subjected for tensile strength test.

***Testing the samples for Surface Roughness**:*

The test samples were subjected to Surface Roughness measuring tester. The samples were mounted on the tester. The diamond point stylus runs back and forth onto the samples and readings of the maximum surface roughness (maximum departure from perfection over a prescribed length) and average roughness (average departure of the surface from perfection over a prescribed sampling length) is displayed on the screen (Figure 1).

The diamond stylus on the surface roughness tester runs across a preset distance and the reading were recorded by a digital meter in terms of Rmax (maximum surface roughness), Ra (average surface roughness),

Testing the samples for Tensile Strength:

The test samples were subjected to a universal testing machine, using a specially fabricated test jig. The samples were supported across two points. Loading was done at a cross-head speed of 0.5 mm/min and the applied load recorded at a chart speed of 20 mm/min. The samples were stretched apart. Loading was continuous until a sudden decrease in the applied load was recorded. This decrease in the load values corresponded to the fracture of the samples. The reading at this particular point was noted down for each test specimen (Figure 2).

SPSS version 22 (statistical package for social sciences) software was used for Statistical analysis. Mean and standard deviation for surface roughness and tensile strength in each group was calculated. One way ANOVA (analysis of variance) followed by Post hoc tukey test was applied for calculating significant differences among 4 groups. P values lower than 0.05 were considered statistically significant in the analysis of the results.

RESULTS:

The mean values and Standard deviation for Maximum Surface Roughness among the four groups was given in (Table 1). The comparison of maximum surface roughness of new alloy showed highly statistically significant difference from recast alloy with F value = 198.43 and p value = 0.001. The Post Hoc Tuckey test shows minimum surface roughness in Group A (Pure alloy) and minimum in Group D (100% Once Recast alloy) with significant difference between groups.

The mean values and Standard deviation for Average Surface Roughness among the four groups was given in (Table 2). The comparison of maximum surface roughness of new alloy showed statistically significant difference from recast alloy with F value = 26.54 and p value = 0.03. The Post Hoc Tuckey test shows minimum surface roughness in Group A (Pure alloy) and minimum in Group D (100% Once Recast alloy) with significant difference between group A with all the alloys.

The comparison of mean values and Standard deviations of Tensile Strength for different groups were shown in (Table 3). The study result found that tensile strength of new alloy showed no statistically significant difference from recast alloy (as p value > 0.05 that is 0.24).

DISCUSSION:

Base metal alloys currently account for a maximum portion of the fixed prosthesis alloy market. The low price of these alloys is the major attraction, although this advantage can be offset by inexperienced handling of the alloys[10]. Two main classes of base metal alloys are the Ni-Cr system and the Co-Cr system. This study was undertaken to evaluate the surface roughness and tensile strength of new alloy and once cast alloy. Aim of the study was to use previously used base metal alloys to produce restorations with minimum cost for the dental laboratories without

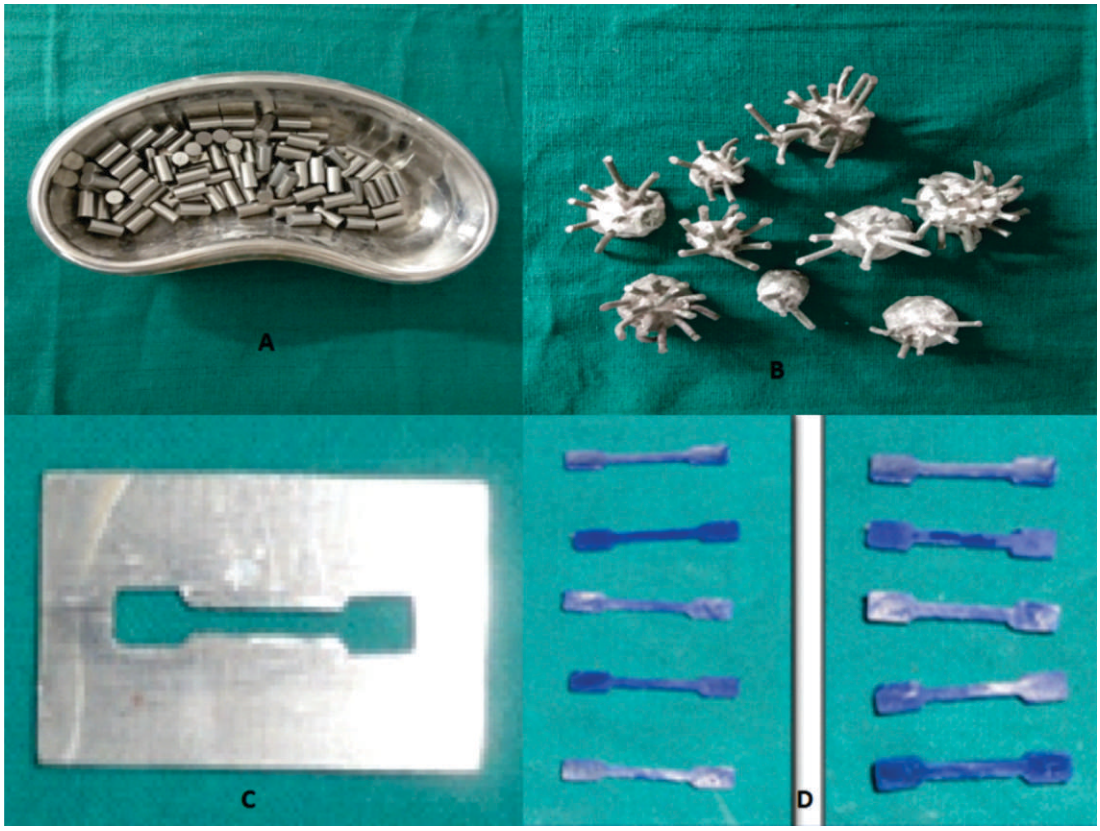

Figure 1: (A) New Alloy (B) Recast alloy (C) Mold for fabrication of test specimen (D) Wax Patterns of Specimen.

Figure 2: (A) Casting Machine (B) Cast Specimen of Alloys© Roughness Tester (D) Test of tensile strength.

Table 1: Comparison between new alloy and recast alloy for maximum surface roughness.

Material	N	Mean	Std. Deviation	f	p value
Group A	30	42.53	4.10		
Group B	30	45.57	4.05		
Group C	30	47.62	4.31	198.43	0.00 *
Group D	30	49.45	3.02		

(p<0.01 highly significant*, p 0.01-0.05 significant, p >0.05 not significant)

Table 2: comparison between new alloy and recast alloy for average surface roughness.

Material	N	Mean	Std. Deviation	Mean Diff	f	p value
Group A	30	4.55	0.83			
Group B	30	4.89	0.85			
Group C	30	5.03	0.85	0.93	26.54	0.03 *
Group D	30	5.49	0.88			

(p<0.01 highly significant, p 0.01-0.05 significant*, p >0.05 not significant)

Table 3: comparison between new alloy and recast alloy for tensile strength.

Material	N	Mean	Std. Deviation	f	p value
Group A	30	4488.40	221.64		
Group B	30	4486.93	250.34		
Group C	30	4487.03	274.17	1.43	0.24 #
Group D	30	4484.20	379.68		

(p<0.01 highly significant, p 0.01-0.05 significant, p>0.05 not significant*)

compromising on the properties of the alloys. For evaluation of surface roughness, samples were mounted onto the surface roughness tester. The diamond stylus on the tester runs across a preset distance and the reading were recorded by a digital meter in terms of Rmax and Ra. Later these samples were mounted on UTM for tensile strength test.

The derived results reveal that there was non-significant difference in tensile strength between Groups. Result also shows consistent increase in maximum Surface Roughness and Average Surface Roughness with the increase in number of recasting. Hesby et al.[11] found no significant alteration in physical properties of alloy after 4 times recasting which is in contrast to our study which found significant increase in surface roughness of recast alloys. They also compared tensile strength first through fourth generations and found were no significant differences in tensile strength of different generation recasting alloys.

The similar result was shown by Agrawal A et al.[12] in which surface roughness significantly increases with recasting but there were non significant difference in tensile strength with recasting of alloy.

James J et al.[13] in 2018 conducted a study divided the metals into 5 groups. Group I included samples casted with new alloy alone. Group II samples consisted of 75% new alloy and 25% once casted alloy. Group III was casted with 50% of each. Group IV with 25% new metal and 75% previous alloy and samples of Group V samples were casted with once casted alloy alone. They found slight variation in mean tensile strength which was statistically insignificant.

However the older studies by Nelson et al[1] in 1986 and Issac & Bhat[14] in 1998 showed significant decrease in Tensile strength on Recasting. Their microstructures showed large amounts of contamination, Porosity, and inclusions, which

increased with each casting generation.

Bandela V and Kanaparthi S[15] in their review article had included 44studies. They founded no changes in mechanical properties on recasting of alloy.

Ronald G. Presswood[7] observed the color and the chemical composition of recast alloys & established no notable change in the composition after six melts of the alloys. So alloy was highly castable but Variations of tensile strength and surface roughness within and among groups were present. The direction and the angle of a sprue attachment may be the possible sources of variations in recorded results.

According to Anusavice[2], the classification of causes for defective castings, one of them is surface roughness and irregularities. The outer surface of the casting necessitates additional efforts in polishing and finishing whereas on the tissue surface prevent a proper seating of casting.

Thus it can be hypothesized by this study that causes for the surface roughness is probably related to the compositional change, micro porosity, loss of certain trace elements[7] such as manganese, chromium and molybdenum, the oxide layer formation[1] and incorporation of oxygen and nitrogen[16].

Surface roughness, readily apparent in all castings of study and is an ever present problem. Castings that contain porosity possess a reduced effective cross-sectional area equal to the size of the defect. These essentially weakened areas affect physical characteristics and alter test results.

CONCLUSION:

Tensile strength of new alloy showed statistically non significant difference on comparison with recast alloy used in 25%, 50% and 100%. However, surface roughness increases as the percentage of recast alloy used for preparation of cast. It is minimum for new alloy, then 25% recast alloy, 50% recast alloy and maximum for 100% recast alloy.

REFERENCES:

1. Donald R. Nelson. Recasting a nickel-chromium alloy. J Prosth Dent 1986 ;Vol 55 No. 1: 122-128.
2. Anusavice KJ. Phillips science of dental materials , 11th Edn. Saunders, St. Louis. 2003.
3. John C. Wataha, Regina L. Messer.Casting alloys. Dent Clin N Am 2004; 48: 499–512.
4. Wataha JC. Alloys for prosthodontic restorations. J Prosthet Dent 2002;87: 351–83.
5. Wataha JC. R.L. Messer.Casting alloys. Dent Clin N Am 2004;48: 499–512.
6. Jayant Palaskar, Dhruv V. Nadgir, Ila Shah. Effect of Recasting of Nickel: Chromium Alloy on its Castability. Journal of Indian Prosthodontics Society:1-5
7. Ronald G. Presswood. Multiple recast of a nickel-chromium-beryllium alloy. J Prosthet Dent 1983;Vol.50 No. 2:198-99
8. Nakhaei MR, Ghanbarzadeh J, Gokharian R The effect of recast base metal alloys on crown's marginal accuracy. J Med Sci 2008; 8:599–602
9. Harcourt HJ, Cotterill WF. Induction Melting of Cobalt-Chromium Alloys; a Comparison with Flame Melting. Br Dent J 1965; 20(11):323-9.
10. Anne-Sophie Vaillant -Corroya, Pascale Corneb PascalDe cSolenne Fleutot dFranck Cleymand. Influence of recasting on the quality of dental alloys: A systematic review. The Journal of Prosthetic Dentistry Volume 114, Issue 2, August 2015, Pages 205-211.e3
11. DA Hesby, P Kobes, DG Garver, GB Pelleu. Physical properties of a repeatedly used nonprecious metal alloy. J Prosthet Dent. 1980;44(3):291–93.
12. Amit Agrawal, Syed W. Hashmi, YogeshRao, Akanksha Garg Evaluation of Surface Roughness and Tensile Strength of Base Metal Alloys Used for Crown and Bridge on Recasting (Recycling). Journal of Clinical and Diagnostic Research. 2015 Jul, Vol-9(7): ZC01-ZC04.
13. James J, Julian J, Rahul J, Philip GB, Devassy JP, Reba PB. Effect of recasting on physical properties of base metal alloys: An in vitro study. Journal of International Society of Preventive & Community Dentistry. 2018 Sep;8(5):457.
14. Issac L, Bhatt S. Effect of reusing nickel chromium alloy on its ultimate tensile strength, yield strength and modulus of elasticity. Indian J Dent Res 1998;9:13–17.
15. Bandela V, Kanaparthi S. Effect of Recasting on the Quality of Dental Alloys: A Review. Inter Medi J. 2021 1;28(1).
16. Maria Peraire et al. Effects of Recasting on the Chemical Composition, Microstructure, Microhardness, and Ion Release of 3 Dental Casting Alloys and Titanium. Int J Prosthodont 2007;20:286–288.

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Evaluate the Effectiveness of Video Assisted Teaching Programme on Knowledge of Infection Control Measures among Nursing Students

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Original Research Article

ABSTRACT

Infectious diseases are continuing threat to all patients, regardless of the age, gender, lifestyle, ethnic background and socioeconomic status. Health care is always facing new danger from incurable infections. Nurses play an important role in the health care team, they need to have current knowledge related to emerging and re-emerging infectious diseases. Student nurses are often exposed to various infections during their clinical experience as a part of curriculum. As a member of health care team, nursing students have huge responsibility to protect themselves, patients and other members of health team.

The aim of the study was to impart the knowledge on infection control measures through video assisted programme among nursing students in order to protect themselves and patients in the clinical field. A quasi-experimental study, one group pre- and posttest design, 150 nursing students was conducted in selected nursing college. Pretest was assessed with demographic profile of nursing students and knowledge questionnaire followed by videos was displayed to the participants regarding specific infection control measures of Hand hygiene and personal protective equipment's (PPE). The post test was conducted after 7 days with same tools used in pretest assessment. The level of knowledge on hand washing technique after video assisted teaching programme on infection control measures increased significantly by 50% in the posttest with mean difference of 2.18,t=14.76 ; the level of knowledge on PPE after video assisted teaching programme on infection control measures increased significantly by 57.4% in the posttest with mean difference of 1.02,t=14.42 at 0.05 level of significant. Statistically significant association between the pretest level of knowledge on hand washing with scores of nursing programme ($x^2 = 39.76$, $p<0.001$), year of experience ($x^2 = 33.19$, $p<0.001$), year of study ($x^2 = 41.35$, $p<0.001$); association between the pretest level of knowledge on PPE with scores of gender ($x = 15.50$, $p<0.001$) nursing programme ($x^2 = 54.07$, $p<0.001$), year of experience ($x^2 = 41.65$, $p<0.001$), year of study ($x^2 = 70.46$, $p<0.001$) was found. Video-assisted teaching programme was effective to enhance the knowledge of hand washing and use of PPE as infection prevention control measures among nursing students in order to protect themselves and patients their practice field and community.

KEY WORDS: hand washing, infection control, knowledge, video assisted teaching programme, personal protective equipment

INTRODUCTION:

Infectious diseases are great threat to all members of health care team and patients regardless of the age, gender, lifestyle, ethnic background and socioeconomic status. They cause suffering, death and impose a financial burden on the society. The history of infection control practices commence to take place in hospitals in 1840 when the importance and influence of hand washing was brought to keen attention in the medical area. Then in 1854, Florence Nightingale was pioneer to document the importance of hygienic environment for good health. Her work is the first ever evidence highlighting the relation of good health to hygienic environmental factors (air, water, light, efficient drainage and cleanliness). Infection control is one of the most important aspects of contemporary hospital management [1].

The World Health Organization (WHO) defined standard precautions as meant to reduce the

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risk of transmission of blood borne and other pathogens from both recognized and unrecognized sources, they are the basic level of infection precautions which are essential in the care of all patients. Nursing has important role in the prevention of infectious diseases in the care of persons and families having infectious diseases[2].

As per the health and safety executive guidelines (1992) on personal protective equipments (PPE), "It is defined as 'all equipment which is intended to be worn or held by a person at work and which protects him against one or more risks to his health or safety". PPE are safety helmets, masks, gloves, eye protection, gown, and safety footwear. It is to paid attention towards the proper fitting PPE, wearing poorly fitting PPE can lead to a number of problems such as excessive sweating, friction, discomfort, also finger and hand muscle fatigue[3].

As per Centers for Disease Control and Prevention (CDC) guidelines (1996) the following standard precautions measures replace the old universal precautions system such as (a) Hand washing: wash hands before and after touching the patients, equipments, patient surfaces, before and after any procedure and immediately whenever required to avoid the transfer of microorganisms. (b) Gloves: Clean and sterile gloves are necessary to wear when touching body fluids, blood, secretions, excretions, and contaminated items. (c) Masks, eye protection, face shields: Masks, eye protection and a face shield to protect mucous membranes of the eyes, nose, and mouth during procedures. (d) Gowns: Clean and sterile gown to protect skin and to prevent soiling of clothing of Health care workers during procedures, exposure to splashes or sprays of blood, body fluids, secretions, or excretions. (e) Patient care equipments: the equipment gets soiled when exposed to blood, body fluids, secretions, and excretions. The equipments used to infected patients, there may be a chance of transfer of microorganisms from one patient to others or to environments. Hence, taking care of patient care equipments, process of cleaning, sterilizing and discarding procedure adopted appropriately. (f) Environmental control: The policies and guidelines of the hospital must ensure the adequate infection prevention and control procedures for the routine care, cleaning of environmental surfaces, taking care of bedside equipment, beds, bed rails, and other frequently touched surfaces, and ensure that these procedures are being followed as per the guidelines/ standard operating procedure or institutional policy[4].

Health care is always facing new danger from incurable infections. Nurses being important role in the health care team, they need to have adequate knowledge and skills regarding emerging and re-emerging infectious diseases. Nurses have to play multidimensional role and their skills have to be combined with a specialized knowledge and practice base to ensure improved health status of the family. Student nurses are often exposed to various infections during their clinical education, and as health care workers, nursing students have huge responsibility to protect themselves, patients and their families from challenging work environment. It is very important for the nurse educators to involve the student nurses in understanding the transmission, risk factors, causes, control and preventive aspects of infectious diseases. The aim of the study to impart the knowledge on infection control measures through video assisted programme among nurses in order to protect themselves and patients their practice field and community.

Statement of the Problem: A study to evaluate the effectiveness of Video Assisted Teaching Programme on knowledge of Infection Control Measures among nursing students. The objectives of the study were to: 1) assess the demographic profile of the nursing students; 2) assess the level of knowledge on hand washing technique before and after video assisted teaching programme on knowledge of infection control measures among nursing students; 3) assess the level of knowledge on use of personal protective measures before and after video assisted teaching programme on knowledge of infection control measures among nursing students; 4) evaluate the effectiveness of video assisted teaching programme on knowledge of infection control measures among nursing students; 5) Associate the demographic profile of the nursing students with pretest level of knowledge on hand washing among nursing students and 6) Associate the background profile of the nursing students with pretest level of knowledge on use of personal protective measures among nursing students.

MATERIALS & METHODS:

The study was aimed to evaluate the effectiveness of video assisted teaching programme on knowledge of infection control measures among nursing students in Bhopal Nursing College, BMHRC, Bhopal. A quantitative research approach and pre-experimental one group pretest and post test research design was used. The sample of 150 nursing students of GNM and Post Basic BSc nursing were the samples of this study. They were recruited through probability

random sampling techniques used in this study. Each group consists of 25 participants. The tools used for data collection were background profile questionnaire, structured questionnaire on hand washing techniques with 10 items and use of personal protective equipments (PPE) with 15 items.

The tools used in this study were validated by nursing and medical experts. Video program on infection control was developed which includes source of infection, routes of transmission, chain of infection, barriers of infection, hand washing technique and wearing - removal (donning and doffing) of PPE. It was edited and structured by members of research team and it was validated by experts. The conceptual framework used in this study was general system theory with input, process and output. The data collection was done from September 2015 to October 2015. The purpose of the study was explained to each candidate. Ethical and administrative permissions obtained from the institution. First day, the pretest data collected with demographic profile questionnaire, structured questionnaire on hand washing techniques with 10 items and use of personal protective equipments (PPE) with 15 items and the same day video assisted teaching programme implemented and after 7th day the post test was conducted with same group by using same questionnaire. The data were analyzed by using descriptive and inferential statistics (Figure 1).

RESULTS:

Among 150 nursing students, 24(16%) students were in the age group of 19 years and majority 112(74.6%) were in the age group of 20 years and above. Majority of the participants 114(74%) were female.130 (86%) undergone GNM course. 20 (14%) belongs to Post Basic Bsc Nursing students (First year). In regards to previous clinical experiences of nursing students, majority, 130(86%) nursing students had no clinical experience, 10(6.6%) had 1-2 years of clinical experience and 10(6.6% had 3-5 years of clinical experience.

The above (Table 1) shows that, before video teaching program the level of knowledge on hand washing was 7.3% (11) and it was increased after the intervention 57.3%(86) ie., the level of knowledge on hand washing technique after video assisted teaching programme on infection control measures increased significantly by 50% in the posttest.

The above (Table 2) shows that before and after video assisted teaching programme on knowledge of hand washing technique , the mean score was

Table 1: Assess the knowledge on hand washing technique before and after video assisted teaching programme on infection control measures (n =150).

Hand washing technique	Inadequate knowledge		Moderate knowledge		Adequate knowledge	
	Frequency	%	Frequency	%	Frequency	%
Before video assisted teaching programme	78	52	61	40.7	11	7.3
After video assisted teaching programme	07	4.66	57	38	86	57.33

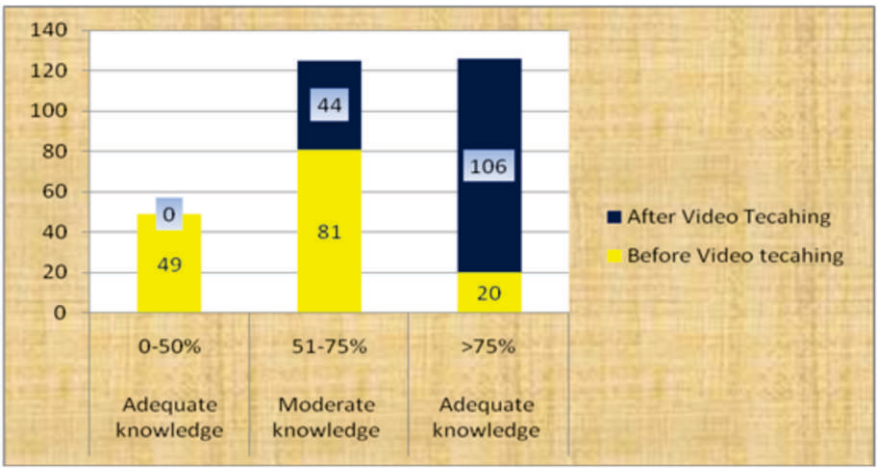

Figure 1: Assess the knowledge on use of PPE before and after video assisted teaching programme on infection control measures.

Table 2: Evaluate the effectiveness of video assisted programme on knowledge of hand washing technique (n=150).

Knowledge on Hand washing technique	Mean score	SD	Difference in mean	t-value
Before video assisted teaching programme	5.44	1.38	2.18	14.76 df=149, p<0.05 level of significance *
After video assisted teaching programme	7.62	1.158		

Table 3: Evaluate the effectiveness of video assisted programme on knowledge of use of PPE (n=150).

Knowledge on Use of PPE	Mean score	SD	Difference in mean	t-value
Before video assisted teaching programme	8.86	2.48	1.02	14.42 df=149, p<0.05 level of significance *
After video assisted teaching programme	12.32	1.50		

5.44, with SD 1.38; mean score was 7.62 and SD 1.158 respectively. Hence the effect of video assisted programme on knowledge of hand washing was found significant at 0.05 level with t value of 14.76. The above (Table 3) shows that, before and after video assisted teaching programme on knowledge of use of PPE, the mean score was 8.86, with SD 2.48; mean score was 12.32 and SD 1.50 respectively. Hence the effect of video assisted programme on knowledge of PPE was found significant at 0.05 level with t value of 14.42.

DISCUSSION:

Associate the background profile of the nursing students with knowledge on hand washing among nursing students. Statistically the significant association between the pretest level of knowledge on hand washing with scores of the type of nursing programme (x2=39.76, df=1), year of experience (x2=33.19,df=4), year of study (x2=41.35,df=6) were significant at 0.05 level of significance and age and gender were not significant.

Associate the background profile of the nursing students with knowledge on use of personal protective measures among nursing students.

Statistically the significant association between the pretest level of knowledge on PPE with scores of the Gender (x2= 15.51, df=1), the type of nursing programme (x2=54.07,df=1), year of experience (x2=41.65,df=4), year of study (x2=70.47,df=6) were significant at 0.05 level.

Implications:

The findings of the study have implications in nursing education , nursing administration and nursing research. Video assisted teaching programme can be incorporated as blended teaching methods to impart the knowledge on infection control. Emphasis on hand washing technique of nurses will reflects on the quality of care. Conduction of inservice education among nurses through video assisted demonstration of hand washing and use of PPE to prevent the infection control measures. It provides the model for teaching to impart the knowledge and can be utilized for the other procedure in the clinical areas.

Recommendations:

Demonstration vs video assisted teaching on knwoldge of hand washing can be conducted. Similar studies with large sample size can be conducted to generalize the study findings. Practice of infection control measures can be measured with structured check list or standardized tool. A comparative study can be done on nurses, nursing students, paramedical staffs and students or with different health care personnel.

CONCLUSION:

A video assisted teaching programme is the effective strategy to improve the knowledge of nursing students on hand washing techniques and use of PPE to prevent the infection and control measures. It ensures the safety of the patients as well as health care personnel. As nurses are the important members of the health care team they must acquaint themselves with adequate knowledge with proper updating to protect themselves and community against infectious diseases.

REFERENCES:

1. Craven RF, Hirnle CJ. J Fundamentals of Nursing: th Human Health and Function. 6th Edn. Philadelphia: Wolters Kluwer Health/ Lippincott Williams & Wilkins, ©2009.pp.56.

2. WHO Guidelines on Hand Hygiene in Health Care (Advanced draft), at: http://www. who.int/patient safety/information_centre/ghhad_download/en/index.html.
3. Personal Protective Equipment at Work Regulations 1992. Guidance on Regulations L25 HSE Books 2005 ISBN 0 7176 6139 3.
4. Centers for Disease Control and Prevention. Hospital Infection Control Practices Advisory Committee. Guideline for isolation precautions in hospitals. Infect Control Hosp Epidemiology. 1996; 17:53-80
5. Daneshwari S, Hiramath. Nurses knowledge of aseptic technique for neonates. Nightingale Nursing Times. 2013; vol. 9(3): pp47.
6. Hema Gogia and Jayanta K Das. Awareness and practice of infection control among doctors and nurses in ICU of a tertiary care hospital in Delhi. Health and population: Perspectives and issues. 2013; 36(1): pp1-11.
7. Garcia Z, Gaimaraes JV, Tipple , Marinesia AP, Macro TA etal. Knowledge and practice of hand washing , use of gloves and handling of disposal of needle stick and other sharp objects among nursing students and medical students . American Journal of India. 2010; 6(1): pp45.
8. Suresh k Sharma. Nursing Research and statistics. Reed Elsevie India pvt Ltd. 2011. First edition.

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Nurses on the Frontline Against the COVID-19 Pandemic: An Experience

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Original Article

BACKGROUND:

Corona virus disease 2019 (COVID-19) was first reported from Wuhan, China in late December 2019 and was declared a global pandemic by the World Health Organization (WHO) on March 11, 2020. As on November 23, 2021, the COVID-19 pandemic has infected more than 256 million individuals globally, leading to 5 million deaths and has disrupted health care systems across the world.[1] Nursing staff, who have always been key frontline health care workers, have been instrumental in the COVID-19 response worldwide, often at the cost of their own physical and emotional well-being[2,3]

The first case of COVID – 19 was reported in India on January 27, 2020, in Kerala, and the first case was diagnosed on March 9, 2020 in MP Central India. In this article, an effort is taken to describe the experience of managing team of nurses who were at the forefront against COVID-19, ably supported by others such as patient navigators, clinical research staff, and administrators.

The selected hospital is one of the hospitals in central India from private sector. Early in the pandemic, the hospital was designated as a COVID-19 hospital for all patients. There is lack of data regarding the impact of the double burden of COVID-19 and shortage of nursing staff in the face of lockdown, other manpower shortage, and personal challenges.

The hospitals began preparations to deal with the pandemic in early March 2020. Several policies were implemented in the hospital to mitigate the risk to staff, patients, and caregivers to ensure effective hospital functioning. The initial preparations included creation of a core action group to review evidence, create and update standard operating procedures (SOPs), and oversee daily operations. Nursing staff were an integral part of this action group and expanded their services beyond routine hours. The action group communicated via a What's App group, and key members of the action group met on a daily basis to review the unfolding situation. The following areas were recognized for urgent action:

1. Screening patients and staff to identify those likely to be infected;
2. Setting up of a fever clinic and facility for testing for COVID-19 and
3. Creation of isolation wards and stepping up the infection prevention control measures.

Subcommittees of the core action group were created to look into each of these aspects. A team of medical staff constantly updated the SOPs based on evolving evidence. Subsequently, when selected hospital became a COVID-19 vaccination center in March 2021, nursing staff took on the additional responsibility of managing the vaccination center.

***Screening of Patients and Staff*:**

One of the measures adopted since March 2020 was screening of patients and accompanying persons at hospital entry points, and thermal screening for hospital staff.

The staff deputed from various departments of the hospital like nursing, paramedical, dental and medical and administration. The identified frontline personnel were rendered intensive training on administering a COVID-19 questionnaire and use of thermal screening to identify high-risk individuals, thus segregating the COVID-19 suspects from others. Those who were identified as high risk- having history of travel, symptoms, high body temperature-were referred to a dedicated "fever clinic" for further evaluation. Others who were screened negative at the entrance were directed to access regular hospital services.

Entry access into the hospital was limited to only one person accompanying the patient, extendable to two if the patient was on a wheelchair. The frontline staff were trained to safeguard themselves from the infection. This training included appropriate use of personal protective equipment (PPE), social

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distancing, and hand hygiene.

Setting up of a Fever Clinic and Facility for Testing for COVID-19:

A section of the main part of the hospital near the entrance was converted to a 'fever clinic' where screened individuals identified as high risk could be evaluated further. Facilities for collecting swabs for reverse transcription polymerase chain reaction (RTPCR) testing, waiting areas for those awaiting the results of the swab, and separate entrance and exit pathways to avoid contacts between suspects and other staff and patients were also set up.

Nursing staff worked in the fever OPD for sample collection, educating the patients and relatives, training other staff and carried out audits. We recognized that hospital staffs, in addition to fulfilling their professional roles, were also concerned about their own safety and that of their families.

Nursing students, having strong professional bond with the selected community, were identified as key members to play the vital role in spreading the right knowledge related to COVID-19 to community and nearby catchment area. Therefore, the process of training nursing undergraduate students and hospital staff on various aspects of COVID-19 started with the objective of educating and guiding the community in that area for reporting to nearby available health facility under Ayushman Bharat.

A group of nursing staff underwent the initial training and then acted as trainers for the other individuals. These training modules were conducted in small batches and included generating awareness about the symptoms of COVID-19, and precautions to be followed by all (respiratory and hand hygiene). In addition, they were taught about infection control practices to be followed in the wards and critical care areas such as appropriate use of PPE, measures to be followed while caring for those with COVID-19, and management of waste disposal.

Periodic audits were performed to assess retention of information and need for retraining.

A separate facility near the hospital was identified as an isolation facility for those with asymptomatic or mild COVID-19, who did not have facilities for home isolation. Within the hospital's existing facilities, new areas were set up by reorganizing various inpatient and outpatient areas to create segregated space for COVID-19 care. An intensive care unit (ICU) facility was created for the patients who required ventilator support and close monitoring. A separate pathway for transport of patients with COVID-19 was identified, rooms for donning and doffing of PPE were set up, and several trial runs were performed much before we had our first patient to ensure that we were well prepared to safely manage patients with COVID-19.

Tracing of Contacts Identifying high-risk contacts of infected individuals is important to minimize the extent of transmission. Nursing staff created a group which had individuals trained in SOPs of contact tracing. The group powerfully conducted interviews of all possible contacts to identify those at high risk. The quarantine facility was set up in the hospital itself, while later on, other premises such as hotels and hostels were used as quarantine facilities. Testing/Retesting of cases and contacts Nursing staff organized by databases of those in isolation and quarantine.

Changes in Working Pattern:

Several changes were adopted to the working pattern of Nursing staff to attend to huge demand and work load in the hospital. The staff with high risk (pregnant, multiple co morbidities, and immune suppressed) were given medical leave during the peak of the pandemic. The staff from medical and surgical areas were retrained in critical care skills and deployed in ICUs. The duration of the shift was increased to 12 hours from eight hours. Monetary benefits too adopted to pay to nurses as 'Covid Allowance'.

Due to shortage of nursing staff, nursing students and faculty from nursing college too were deployed in the hospital. Due to acute shortage of nursing staff, 'Buddy concept' could not be implemented where staff is deployed to 'non covid' area, where PPE not required, in shifts alternatively. The much required 'OFF' too could not be provided to nursing staff due to acute shortage.

This lead to many adjustments and physiological problems among the nursing staff. They started vocalizing their problems and difficulties faced by them. Few refused to work straight away and many started remaining absent in allotted shift. This absenteeism was managed by deploying nursing students of final years (IV and III B Sc Nursing) after convincing their parents and assuring them that their ward will be protected and will be looked after well. A transport too was arranged to pick and drop them for night shift.

It was found that most of the nurses had the responsibility to look after their family viz few had ailing old parents (15 %), few had very small babies to look after (25%)and few had to cook (45%) as home aid also was not available due to lock down, few abstain themselves due to social stigma from neighbors and

family (10%), remaining 05% did not verbalize the reason for remaining absent. Most of the nurses who used PPE for prolonged periods reported various types of injuries.

Many a times it happened so that the nurses did not report in night shift (33%). Many a times the nursing staff on evening shift was requested to carry on with the night shift too (22%).

The role of the nursing team in dealing with the pandemic has been acknowledged by the hospital administration as one of the most essential aspects of the generally response. Nurses presented their observations and learning in hospital meetings, in National and International webinars, to allow others to benefit from their experience.

DISCUSSION:

The WHO estimates that 80,000 to 180,000 health care workers could have died with COVID-19 between January 2020 and May 2021.[3]

Several of them are likely to have been nursing staff. Bandyopadhyay et al looked at COVID-19 infections and deaths among health care workers and found that among those infected, nurses constituted the largest proportion (38%).[4] The impact of the pandemic on the mental health of nurses has also been well documented, with several studies reporting anxiety, depression, stress, burnout among nursing staff. [5] A systematic review and me ta-analysis looking at psychological distress among health care providers during COVID-19 in Asia establish that more than one-third of healthiness care providers suffered from anxiety and depression, the likelihood being higher with female gender. [6] Lack of human and physical resources and the number of colleagues infected with COVID-19 were the strongest predictors of stress, anxiety, and depression among nurses.[7] India and found that 12 to 14% of them reported anxiety and depression among frontline nurses.[8] Nurses have been at the receiving end of bullying and social stigma due to the perception that they are carriers of COVID-19. In a study among health care workers in India, Radhakrishnan et al found that 70% of nurses reported a stigmatizing experience during COVID-19, and that being a nurse and working in a clinical area were more likely to worsen this experience.[9] Most of these reports are from the initial period of the pandemic where transmission was less understood and fear was high. After several months into the pandemic, and recognizing the vital role that health care workers have played, such problems and stigma do not exist anymore.

a stigmatizing experience during COVID-19, and that being a nurse and working in a clinical area were more likely to worsen this experience.[9] Most of these reports are from the initial period of the pandemic where transmission was less understood and fear was high. After several months into the pandemic, and recognizing the vital role that health care workers have played, such problems and stigma do not exist anymore.

The use of PPE is associated with problems such as pressure, headaches, sweating, disturbances of vision, and difficulty in breathing. It has been estimated that three out of four individuals who use PPE are likely to have adverse events related to skin.[10] Nurses, due to their long-duration shifts and fixed postings in COVID-19 wards, are more likely to experience such problems. Wearing PPE for longer than 4 hours has been identified as a significant factor for adverse events, and limiting the duration of PPE to less than 4 hours could be the solution.[11] The training of nursing students during the pandemic has also been affected, during pandemic the classes were suspended completely and students were called for clinical duties in the hospital.

Nurses have always been a part of a multidisciplinary team and recognize the importance of teamwork through collaboration and good communication. During the pandemic, the nursing staff has taken teamwork to new heights and worked in close partnership with several other departments —patient navigation teams, administration, medical staff, clinical research staff, and many others.[12,13]

CONCLUSION:

The WHO had designated the year 2020 as the 'year of the nurse and midwife', in the honor of the 200th birth anniversary of Florence Nightingale. It is appropriate that in this year, nurses have been the champions in the battle against COVID-19. However, in the course of this battle, nursing staff have faced several challenges which need to be addressed to ensure their continued well-being. Health Care administrations should recognize the critical role that nurses play in crisis situations and empower them while they deliver important aspects of the overall response.

REFERENCES:

1 WHO. COVID-19 dashboard. World Health Organization. Accessed November 23, 2021 at: https://covid19.who.int/

2 Varghese A, George G, Kondaguli SV, Naser AY, Khakha DC, Chatterji R. Decline in the mental health of nurses across the globe during COVID-19: a systematic review

and meta-analysis. J Glob Health. 2021;11:05009.
3 Bandyopadhyay S, Baticulon RE, Kadhum M, et al. Infection and mortality of healthcare workers worldwide from COVID-19: a systematic review. BMJ Glob Health. 2020;5(12):e003097.
4 WHO and partners call for action to better protect health and care workers from COVID-19. World Health Organization. Accessed February 3, 2022 at: https://www.who.int/news/item/21-10-2021- who-and-partners-call-for-action-to-better-protect-health-and-careworkers-from-covid-19#:~:text¼In %20a%20Joint%20Statement%20 issued,among%20health%20and%20care%20workers
5 Barrett D, Heale R. COVID-19: reflections on its impact on nursing. Evid Based Nurs 2021;24(04):112–113.
6 Chen SC, Lai YH, Tsay SL. Nursing perspectives on the impacts of COVID-19. J Nurs Res 2020;28(03):e85.
7 Baraka AAE, Ramadan FH, Hassan EA. Predictors of critical care nurses' stress, anxiety, and depression in response to COVID-19 pandemic. Nurs Crit Care 2021 (e-pub ahead of print). Doi: 10.1111/nicc.12708.
8 Sharma SK, Mudgal SK, Thakur K, Parihar A, Chundawat DS, Joshi J. Anxiety, depression and quality of life (QOL) related to COVID-19 among frontline health care professionals: a multicentric crosssectional survey. J Family Med Prim Care. 2021;10(03): 1383 –1389.
9 Radhakrishnan RV, Jain M, Mohanty CR, et al. The perceived social stigma, self-esteem, and its determinants among the health care professionals working in India during COVID 19 pandemic. Med J Armed Forces India. 2021;77(Suppl 2):S450–S458.
10 Montero-Vilchez T, Cuenca-Barrales C, Martinez-Lopez A, MolinaLeyva A, Arias-Santiago S. Skin adverse events related to personal protective equipment: a systematic review and meta-analysis. J Eur Acad Dermatol Venereol. 2021;35(10):1994–2006.
11 Atay S, Cura ŞÜ Problems encountered by nurses due to the use of personal protective equipment during the coronavirus pandemic: results of a survey. Wound Manag Prev. 2020;66(10):12–16.
12 Mulyadi M, Tonapa SI, Luneto S, Lin WT, Lee BO. Prevalence of mental health problems and sleep disturbances in nursing students during the COVID-19 pandemic: a systematic review and meta-analysis. Nurse Educ Pract 2021;57:103228.
13 Singh HK, Joshi A, Malepati RN, et al. A survey of e-learning methods in nursing and medical education during COVID-19 pandemic in India. Nurse Educ Today. 2021;99:104796.A

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Exclusive Modified Constraint-Induced Movement Therapy for Motor Recovery in Left Hemiplegic Patient

Case Report

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ABSTRACT

Chronic hemiplegics are a big challenge for the therapist to restore their motor skills and the patient survives with poor quality of life and dependency. The study reports a case study on the response of chronic left hemiplegic patient focusing on the role of unique modified Constraint-Induced Movement Therapy as an intervention that doesn't respond to the conventional approach. The detail of how the patient progressed in the motor improvement of the paralytic upper limb is discussed. A convergent association of mCIMT& Task-oriented approach has been demonstrated as a success story for post-stroke recovery in a short period of 4 weeks and in kicking off Neuroplasticity.

KEY WORDS: chronic hemiplegia, paralytic upper limb, upper extremity, post stroke, rehabilitation, physiotherapy, modified constraint induced movement therapy, conventional therapy, learned nonuse, motor recovery, case report

INTRODUCTION:

Stroke/ Cerebro-vascular Accidents is a medical emergency where there is a high mortality rate and the patient shall survive with devastating paralysis shall occur. The condition shall occur due to reduced or obstruction of blood supply to the brain. It could be ischemic, hemorrhagic, and/ or Transient Ischemic Condition. The brain deprived of oxygen and glucose through blood shall damage due to poor nutrition.

The pathology of stroke is relatively similar to the heart attack, where blood flow is disturbed due to ischemia and/ or necrosis leading to the death of peripheral tissues and so the condition is also known as Brain Attack. Mainly Stroke apart from Transient Ischemic Attacks results in enduring damage that accounts for death or severe sensory-motor deficits.

A systematic review is done by Sureshkumar Kamalakannan et al (2017) on the prevalence of Stroke in India exhibits that the incidence ranges from 105-152/ 100000 persons yearly. This value is alarming as they are very high compared to high-income countries. The review was focused on the magnitude of stroke in the country from 2000-2008 in association to 1970-1979 studies.

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Hemiplegia: Contra-lateral weakness of one side upper and lower extremities is a common post Stroke presentation. Facial muscles shall also be involved in such cases. American National Stroke Association had estimated about 90% of Stroke survivors shall have Hemiplegia. One side stroke of the brain shall lead to opposite side hemiplegia as most of the motor fibers cross to the opposite side of the cerebral cortex. Restricted movement with sensory loss shall lead to reduced activity of daily living and even dependency on others. Poor musculature shall also contribute to in-coordination, poor balance, circumduction gait, difficulty to grasp, etc. these presentations could be worse by complications like Reflux Sympathetic Syndrome, Shoulder subluxation, uncontrolled Spasticity, etc.

Rehabilitation of hemiplegic patients involves a multidisciplinary team involving a Physiotherapist, Occupational therapist, Speech therapist, Nutritionist, Vocational officer, etc. There is no substitute for therapy and effective approaches shall provide promising results. Physiotherapy is one of the prime interventions that take care of the sensory-motor recovery of the hemiplegic side. Conventional therapies like ROM exercises, Coordination & balance training, Task orientation approaches and

Neurodevelopment techniques shall improve the voluntary control of the patient. The latest approaches are also effective in targeted groups. These advanced techniques are Functional Electrical Stimulation, Motor Imagery, Mirror Therapy, Wii Therapy, Robotics Exercises and Bio-feed Back Therapy. Assistive devices, splints and/ or a wheelchair are administrated in feebly prognostic cases.

Neuroplasticity is a phenomenon that occurs due to intense therapeutic approaches. Cortical plasticity, Brain rewiring, Neural Adaptation, etc were different terms used to describe the spontaneous alteration of the brain that takes over the functions of damaged areas and brings motor recovery or functional independence to the patient. Lots of studies are conducted to streamline the interventions and their modified protocols on enhancing Neuroplasticity in patients with Upper Motor Neuron Lesion. Though interventions stimulate, multiple mechanisms work physiologically at the brain in the process of recovery and Brain plasticity. Principles like Use it or lose it, specificity, Repetition, Intensity, Duration, Interference, Transference, etc of various interventions shall play a key role in Cortical Plasticity. Optimizing the principles of plasticity Physiotherapists can play a vital role in improving the patient's quality of life. Researches conducted on such interventions are also focused on cost-effective and early recovery competent approaches.

Chronic Hemiplegia that is more than 02 years from the onset of injury shall go to the Residual Spasticity Stage. In Upper motor neuron lesions like stroke, the muscles turn into spasticity. This shall restrict the voluntary movement and the muscles shall characterize by a velocity-dependent increase in tonic stretch reflexes. This condition gradually moves to muscle fibrosis and permanent deformity, if not rehabilitated. The development shall occur after 2 years duration. At this stage, no therapeutic interventions usually work for the patient and the chances for Neuroplasticity decline. Most of these hemiplegics suffer from upper limb impairment which shall be lifelong restraint.

Constraint-Induced Movement Therapy (CIMT) is known to the therapy community as an approach to chronic stroke patients in improving upper limb function. The technique developed by Dr.Edward Taub, a behavioral neuroscientist is studied effectively in Cerebral palsy, Brain injury and Stroke patients with hemiplegia. This technique is intended to decrease the effect of "learned Non-use". Patients who are medically stable and in a better Neuro-muscular condition shall be benefitted from the program. CIMT works by constraining the normal side with splints/ POP and forced use of the affected upper limb for about 6 hours a day. The therapist needs to provide continuous feedback and the patient needs to be committed to the activity section. Limitations for CIMT are physiotherapists need to spare a lot of energy time and resources, whereas patients shall feel worn out with intense and prolonged exercise sections. Besides, that therapist is also worried about the patients falling in line and about some patient safety issues.

Modified Constraint-Induced Movement Therapy (m-CIMT) is subjectively developed by the therapist at their patient's convenience. A lot of efforts is done by physiotherapists recently to refine CIMT parameters and to advance it as per ease of hemiplegics. The duration and/or intensity of constraining the unaffected side and that of the paralytic arm were more on focus in m-CIMT. The clinical experts around the world are working for the refined approach as m-CIMT is cost-effective and easy to intervene even in the home environment. Focus is also on patient self-motivational interventions and psychological endorsement.

OBJECTIVE OF THE STUDY:

To highlight the outcome of the unique protocol of modified Constraint-Induced Movement Therapy (m-CIMT) in upper extremity motor recovery of a hemiplegic patient.

CASE DESCRIPTION:

The subject of this study is a 66-year-old male from Central India diagnosed with right Middle Cerebral Artery (MCA) Stroke 3 ½ years before, in 2016. The patient has then admitted to the hospital had emergency medications and preliminary Physiotherapy. As he managed to walk with partial support, he got discharged and run down from further therapy.

The subject later approached the researcher for impaired hand functions, poor balance and gait. Balance and Gait of the left hemiplegic patient were an easy goal to accomplish as these purposes are already healthier. But upper limb functions were quite compromised. After 6 weeks of continued conventional therapy, the upper extremity remained almost impaired. It was a big challenge for a physiotherapist to overcome the "Learned Non-use" of the affected limb. Moreover, Middle Cerebral Artery Stroke had severe upper limb involvement related to the lower extremity.

3½ years older neglected Stroke muscle responses shall be underprivileged. "But I have promises to keep, And miles to go before I sleep." The lines of Robert Frost remind you to take a leap ahead and to explore unheeded to keep the promise to the patient.

On examination, superficial sensations and proprioception of the affected hand were almost intact. Passive ROMs of the Wrist and Elbow were almost full. End range restrictions were there for shoulder abduction and external rotation. Muscle power arrays from 3 to 4 in various joints. He was well oriented and the higher functions were normal. Functional evaluation was done on upper limb motor serving of Fugl Meyer Assessment Scale for Stroke. Out of 66 for upper limb motor function, the patient had scored 26, from 33 items on the pre-test.

The Intervention was finalized after a detailed review of various pieces of literature and studies; **modified Constraint-Induced Movement Therapy (m-CIMT)** was confirmed. The patient had already undergone 2 months of physiotherapy and improved Balance, coordination and Gait. But upper limb functions of the hemiplegic side don't respond well. An exclusive m-CIMT program was structured for the subject with the following parameters:

* Maximum of 1½ hours per sitting and two sections per day.
* A long pan splint was used as the constrain material for normal hand (right side).
* The restraint was recommended during the treatment duration and of additional 3 hours apart on busy hours.
* Motor Relearning Program and Task-oriented approaches were used for left upper limb (non-dominant side) rehabilitation for the said therapeutic duration.
* The participant had undergone the treatment for 6 days a week for 4 weeks.

The intervention was carried on a patient's home setup and was conducted during October-November 2019.

The patient was counseled and well-motivated for active contribution during the program. The self-dive of the subject for the given target achievement time of 4 weeks was very well commendable. Continued feedback and appreciation worked with the eagerness and hard work of the patient. Post-test with upper limb portion of Fugl Meyer Assessment scale was done on the last day of the second and fourth week. The total scores were 33 and 53 respectively for the second and fourth week.

RESULTS:

The motor response was recorded pre and post-test by Fugl Meyer Assessment Scale (FMA). Post-test was repeated at the end of the second and fourth week for the paralytic upper limb. Heaps of positive responses were recorded for the patient at the end of the fourth week, post-intervention for the patient.

FMA for upper limb motor functions score of the subject repeated on the first day (Pre-test), end of the second week (on the course) and end of the fourth week (post-test). The scores obtained were detailed on the following chart (Table 1).

The graph of the FMA score (Figure 1) also displays a clear picture of how individual criteria responded to the intervention, m-CIMT, from day one to the end of the second and fourth week in comparison to maximum scores.

The above chart describes how the patient's condition had matured through the course of treatment. The chat displays the better prognosis in upper limb, hand and coordination categories, whereas responses were not satisfactory in wrist criteria.

Overall motor prognosis in the second week was not satisfactory, but the responses were remarkable at the end of the fourth week.

DISCUSSION:

The prime intention of the study was to know whether exclusively designed modified Constraint-Induced Movement Therapy (m-CIMT) works for the hemiplegic patient. The subject's paralytic upper limb doesn't work for conventional Physiotherapy and then he was administrated with the m-CIMT.

The entire study program of the m-CIMT was done for 4 weeks, where pre-test was done before the intervention and post-test were done on the second and fourth week by Fugl Meyar assessment scale for the post-stroke patient. The total motor portion of FMA is categorized as upper limb synergy/ activity, Wrist stability, Hand functions and Coordination & speed of the upper limb. The second week's responses in all the criteria were not satisfactory, but these picked up well by the end of the fourth week. This could be due to the patient's time taken to assume the new approach and to get actively involved. Feedback and motivation in the first phase had shown a low response.

The upper limb and coordination functions improved enormously. Whereas wrist and hand functions evolutions were comparatively poor. This could be to their complexity in motor activity and time-

Table 1: The subject's scores on FMA.

Sl.No	part	Max. Score	Score on1st day	Score at the end of II week	Score at the end of IV week
A	Upper limb	36	16	20	32
B	Wrist	10	03	04	06
C	Hand	14	03	05	09
D	Coordination/ speed	06	04	04	06
A-D	Total A -D (motor functions)	66	26	33	53

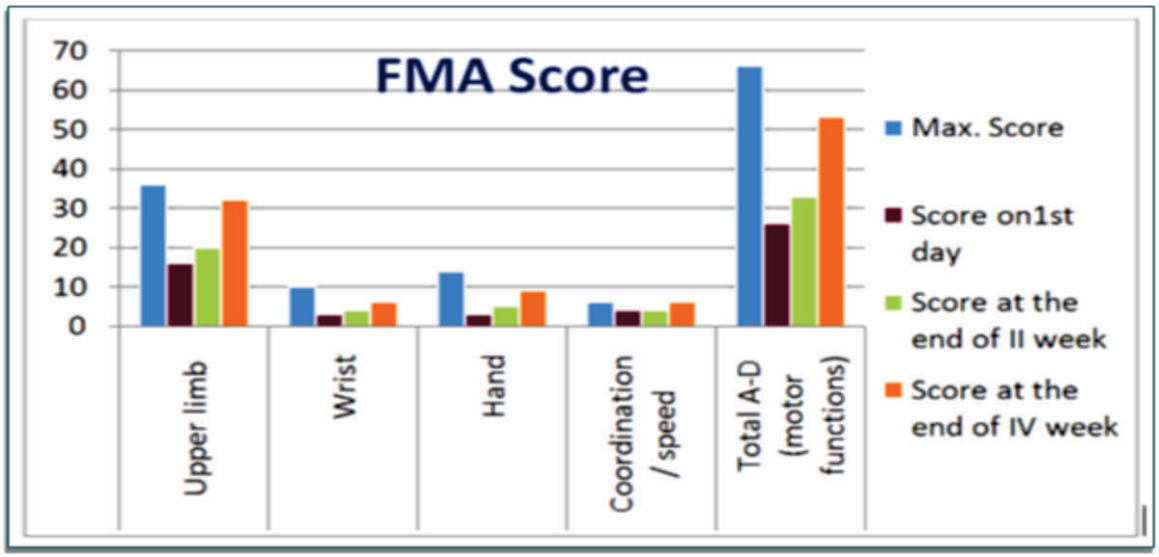

Figure 1: Comparison of FMA scores.

consuming more for the Neuroplasticity. Larger joints responded well with better coordination and/ or speed. The subject had initially shown some distress on wearing the pan splint for about 6 hours a day. However, he had engrossed in the tactic of the program and expressed his interest in achieving maximum motor recovery. This indicates that physical intervention with psychological endorsement was working well for the patient. During the said course no side effects were reported, though the patient complained about some discomfort during the early stage which relinquish by itself in few days.

The patient before receiving m-CIMT was undergoing conventional Physiotherapy for about 2 months, which could not break "Learned nonuse". But this long-established section would have conditioned the limb to be prepared for m-CIMT. Spasticity of the limb was in control; ROMs of upper extremity joints were almost normal and the muscle power were 2-4 in most of the parts. All these had facilitated the speedy response when m-CIMT was applied.

The results demonstrate high significance of exclusively designed m-CIMT working for the subject. Utmost of 1½ hour per sitting twice a day is worthful. Long pan splint used as constraining material for sound hand (right side) managed the purpose successively. Motor Relearning Program and Task-oriented approaches were used for left upper limb rehabilitation were of enormous exercise. The total duration of the said program was of 4 weeks, 6 days in a week was result-oriented. In short, this unique protocol of m-CIMT is objective-directed for the patient.

The study concluded in 4 weeks and no further intervention and/ or follow-ups were done, which is a major deficiency in the conformation of the sustained effect of the approach. The single-subject – case report can't be comprehensive, but if it could shed new light on some researchers to carry forward with randomized

control trials in large groups, then this submission shall pull off its intention.

CONCLUSION:

The clinical relevance of the study is that it has highlighted chronic hemiplegic patient's considerable response to the exclusively designed m-CIMT, which overcomes the paralysis that doesn't respond to conventional therapy. The future study shall be done on a larger group, with a randomized controlled trial for the confirmation of the effect of the unique m-CIMT program. Further such studies shall also focus on m-CIMT in a sundry environment and for conditions like Cerebral palsy, Traumatic brain injury, etc with hemiplegia.

REFERENCES:

1. Gilroy J. Basic Neurology, 3rd (Edn.); McGraw-Hill, New York, 2000.
2. Hachinski V, Norris J. The Acute Stroke. FA Davis, Philadelphia, 1985.
3. Curtis S, Porth C. Disorders of brain function. In Porth, C (Edn.): 5, Pathophysiology, Lippincott (Edt), Philadelphia, 1998,p 879.
4. Haig A, et al. Locked-in syndrome: A review. Curr Concepts Rehabil Med . 1986;2:12, .
5. Haig A, et al. Mortality and complications of the locked-in syndrome. Arch Phys Med Rehabil. 1987;68:24.
6. Kaplan P, Cailliet R, Kaplan C. Rehabilitation of Stroke. Butterworth-Heinemann, Woburn, MA, 2003.
7. Bogousslavsky J, et al. The Lausanne stroke registry: Analysis of 1,000 consecutive stroke patients. Stroke. 1988;19: 1083.
8. Neurological disease, pg no. 1200 (stroke)
9. Smith D, et al. Proprioception and spatial neglect after stroke. Age Ageing. 1983;12:63.
10. Fields H. Pain. McGraw-Hill, New York, 1987.
11. Glowlla F, Golwalla SA. Medicine for Students, chapter-6 Neurology. 2008. pg no. 516 (stroke).
12. Anil Dixit, Yatharth Dixit, Anil Mishra. Basics of Community Medicine. Vol 1; Chapter 6 Epidemiology of Non-Communicable Disease. 2020: 265.
13. George Mathew K, Aggarwal P. Medicine (manual for undergraduates) chapter 5 disease of the nervous system.2008. pg no. 245.
14. Thorn GW, Fauci SA, Eugene braunwal-ddenniskasper, Harrison's Principles of Interrnal Medicine, chapter 346 Cerebrovascular Disease. 2008. pg no. 2513& pg no. 2549.
15. Swash M, Lynn MG. Hutchison's Clinical Methods (an integrated approach to clinical practice), chapter-10 Nervous system. 2007. pg no.- 207.
16. Mehta PT, Mehta SP, Joshi SR. Practical Medicine, chapter- 6 central nervous system. 2009. pg no.288.
17. Davidson S, Boon N, Nicki R. College, Davidson Principles &Practice of medicine. 2006. chapter 26.
18. Twitchell, T. The restoration of motor function following hemiplegia in man. Brain. 1951;47:443.
19. Brunnstrom, S. Motor testing procedures in hemiplegia based on recovery stages. J Am Phys Ther Assoc. 1966;46:357.
20. Bobath B. Adult Hemiplegia: Evaluation and Treatment, 2nd (Edn.); Heinemann, London, 1978.
21. Fugl-Meyer A, et al. The post stroke hemiplegic patient, 1. A method for evaluation of physical performance. Scand J Rehabil Med. 1976;7:13.
22. Gray C, et al: Motor recovery following acute stroke. Age Ageing. 1990;19:179.

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Development and Characterization of Deflazacort Nanoparticles for the Treatment of Inflammatory Bowel Disease

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ABSTRACT

Inflammatory Bowel Disease (IBD) are difficult to control and the reappearance is the most challenging issue for the physicians. IBD includes Ulcerative colitis (UC) and Crohn's disease (CD) .There are various controlled and colon targeted drug delivery systems available for the treatment with a limited success rate. Nanoparticles prepared by using the colon targeted polymers such as chitosan may improve the condition of IBD due to their smaller size, unique physicochemical properties, and targeting potential. Deflazacort is a glucocorticoid used as an anti-inflammatory, immunosuppressant and commonly prescribed drug for the patient having IBD such as Ulcerative Colitis (UC) and Crohn's Disease (CD). The purpose of the present study was to prepare and evaluate the potential of eudragit coated chitosan nanoparticles of Deflazacort for the treatment of IBD by ionic gelation method. These nanoparticles were further coated with Eudragit S-100 by the solvent evaporation technique so as to prevent drug release in the stomach and small intestine. Developed Nanoparticles were subjected to various characterization tsechniques such as FTIR, particle size, scanning electron microscopy (SEM), drug entrapment efficiency and zeta potential. The efficiency of drug release from prepared formulation was studied in vitro in gastrointestinal fluids of different pH. The prepared nanoparticles demonstrated the size in the nano range. The release pattern of Deflazacort from eudragit-coated chitosan nanoparticles was observed to be pH dependent. In acidic medium, the release rate was much slower however the drug was released quickly at pH 6.8 and 7.5. Subsequently, stability study at various storage temperature was also done in which the prepared formulation showed improved stability. The zeta potential of the best chitosan preparation (F2) was found to be -30.5 mV, which confirms the stability of prepared nanosuspension. Eudragit-coated chitosan nanoparticles can be a promising carrier for colon-targeted delivery of Deflazacort found to have high encapsulation efficiency and predetermined in vitro drug release profile.

KEY WORDS: Inflammatory Bowel Disease, Deflazacort, ionic gelation method, eudragit-coated

INTRODUCTION:

Deflazacort (1-(1,16)-21-(acetyloxy)-11-hydroxyl-2-methyl-5H-pregna-1,4-dieno[17,16-d] oxazole-3, 20-dione) is a synthetic glucocorticoid and an oxazoline derivative of Prednisolone. It has influential anti-inflammatory activity and immunosuppressive action[1-2], which is quite analogous to Prednisolone. Deflazacort is a prodrug and is utilized in Duchenne muscular dystrophy (DMD), Rheumatic polymyalgia, Drug-resistant epilepsy of childhood, Idiopathic Nephrotic Syndrome (INS), renal transplant and Asthma [3]. In India it is sold under the trade name as Moaid, Zenflav, Defolet, DFZ, Decotaz, and DefZot. The oral route of drug administration is the most convenient and hence the preferred means of drug delivery to the systemic circulation of the body. However, oral administration of most drugs in conventional dosage forms has limitations due to their inability to restrain and localize the drug delivery system at GIT.

Because of smaller size and efficient carrier capacity, Nanotechnology is now becoming an important area of research due to its wide range of benefits in the pharmaceutical industry and applied sciences [4,5]. Recent research reports revealed the opportunities of nanomedicine in the treatment of IBD. Nanomedicine may replace the conventional dosage forms in the treatment of IBD[6]. Present treatment of IBD lacks cure (only remission). Nanoparticles are helpful in improving the function of current existing drugs by targeting action, solubility improvement and

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dose reduction [7]. Various study reports revealed the advantage of nanoformulations for IBD at minimum doses[8]. Chitosan nanoparticles have gained significant importance since chitosan is the natural colon targeted polymer. Because of its biocompatible properties, chitosan was gravely investigated as a potential drug carrier and is a natural linear biopolyaminosaccharide obtained by alkaline deacetylation of chitin, the second abundant polysaccharide next to cellulose[9]. Some studies have suggested utilizing chitosan to coat nanoparticles made of other materials to lower down their impact on the body and increase their bioavailability.

The elemental composition of the chitosan polymer is carbon (44.11%), hydrogen (6.84%) and nitrogen (7.97), because of their biocompatibility , biodegradability, low immunogenicity and low cost, chitosan has emerged as an important biomaterial and pharmaceutical excipient for drug delivery[10].

The formation of chitosan nanoparticles includes a simple and non toxic method known as ionic gelation method. In this method, chitosan polysaccharide is dissolved in aqueous acidic solution to get the cation of chitosan[11]. The solution formed is then added to the aqueous Sodium tripolyphosphate [STPP] solution under stirring conditions. In this research work, Deflazacort nanoparticles were prepared by high result oriented ionic gelation method with some slight modifications. Chitosan was utilized along with STPP. The formulations are developed with a scope of better therapeutic efficacy, solubility and penetration at the inflamed site.

MATERIALS & METHODS:

Chitosan, Eudragit S-100 was obtained from HiMedia Laboratories Ltd, Mumbai, India. STPP, acetic acid, ethanol, Span 80, acetone, dichloro-methane and light liquid paraffin were purchased from Central Drug House Pvt Ltd, Mumbai, India. All other reagents and chemicals used were of analytical grade.

Preformulation Studies:

Solubility:

The Solubility of the drug was determined by weighing approximately 10 mg of drug and transferred to 7 different volumetric flask of 10 ml. Different solvents (Distilled water, 0.1 N HCl, 0.1 N NaOH, Ethanol, Methanol, pH 7.2 phosphate buffer and Chloroform) were made up to mark into the 10 ml flask respectively and shaked vigrously. The solubility was observed at room temperature.

FTIR spectroscopy:

IR spectra of physical mixture of drug and excipients were recorded by KBr method using Fourier Transform Infrared Spectrophotometer. A base line correction was made using dried potassium bromide pellet. The potassium bromide-drug pellet of approximately 1 mm diameter, was prepared by grinding 3-5 mg of physical mixture of drug-excipients with 100-150 mg of potassium bromide in pressure compression machine. The sample pellet was mounted in IR compartment and scanned at wavelengths 4000 cm-1 to 400 cm-1.

Determination of λ_{max} of Deflazacort:

Accurately weighed 10 mg of drug was dissolved in 100 ml of phosphate buffer pH 7.2 in a 100 ml volumetric flask. 0.1 ml of this stock solution was pipetted into a 10 ml volumetric flask and volume was made up to the mark with phosphate buffer pH 7.2. The resulting solution was scanned between 200-400 nm using UV/Vis double beam spectrophoto-meter. The same procedure was followed for determining the wavelength maxima phosphate buffer pH 7.2.

Fabrication of Deflazacort loaded nanopar-ticles by ionic gelation technique:

Chitosan nanoparticles were prepared by Ionic gelation method. Chitosan stock solution (1% w/v) was prepared by dissolving chitosan in acetic acid (1% v/v) in a beaker at room temperature. The 5mg of drug Deflazacort was dissolved in chitosan solution in a beaker for around five minutes with the help of a bath sonicator (Indian Machine tools, India). STPP solution (1%) was prepared separately in distilled water. Chitosan nanoparticles were fabricated with the dropwise addition of STTP solution with the help of a syringe to chitosan solution under magnetic stirring at room temperature. The solution was magnetically stirred for half an hour followed by filtration and rinsing with distilled water. The acquired Nano-particles were air dried for twenty four hours followed by oven drying for six hours at 40˚C[12]. The compo-sition of chitosan nanoparticles is given (Table 1).

Coating of prepared nanoparticles:

With the aid of solvent evaporation method, chitosan nanoparticles were coated with Eudragit S-100 (ES). In 10ml of the coating solution prepared by dissolving 500 mg of ES-100 in ethanol, 50 mg of nanoparticles were dispersed: acetone (2:1) to give 5:1 (coat: core ratio). Subsequently, this organic process was poured in light liquid paraffin containing 1% w/v

Table 1: Formulations of chitosan nanoparticles.

Formulation Code	Deflazacort (mg)	Chitosan (mg)	STPP (mg)
F1	5	250	500
F2	5	250	750
F3	5	250	1000
F4	5	500	500
F5	5	500	750
F6	5	500	1000

Span 80. The system was maintained for 3 hours at room temperature under agitation speed of 1000 rpm which allows the solvent to evaporate. The coated nanoparticles coating were filtered, washed with n-hexane and dried in desiccators[13].

Evaluation of nanoparticles:

Drug Entrapment Efficiency-

Deflazacort was estimated in Chitosan nanoparticles by ultra centrifugation method. The 10mg of formulation was transferred to 10 ml centrifuge tube and diluted with distilled 10 ml of phosphate buffer (pH 7.2) and centrifuged at 2000 rpm for 20 minutes to separate out undissolved drug in the formulation. Supernatent and nanoparticles (sediment) was recovered and their volume was measured. Nanoparticles was diluted with distilled water upto 5ml. The unentrapped and entrapped drug contents were analyzed by estimating drug in supernatant and nanoparticles by spectroscopic method. The percentage of drug entrapment and yield was calculated as:

% drug entrapment = calculated drug content / theoretical drug content ×100

Measurement of mean particle size-

The mean particle size of the nanoparticles was determined by Photo Correlation Spectroscopy (PCS) on a submicron particle size analyzer (Malvern particle size analyzer) at a scattering angle of 90°. A sample (0.5mg) of the nanoparticles was dragged in 5 ml of distilled water which was used for the measurement.

Determination of zeta potential-

The zeta potential of the drug-loaded nanoparticles was measured on a zeta sizer (Malvern particle size analyser) by determining the electrophoretic mobility in a micro electrophoresis flow cell. All the samples were measured in water at 25°C in triplicate.

Shape and surface morphology-

From the formulated batches of nanoparticles, formulations (F2) which exhibited an appropriate balance between the percentage of drug releases was examined for shape and surface morphology with the help of a scanning electron microscope (Jeol Japan 6000). The Sample was fixed on carbon tape and fine gold sputtering was applied in a high vacuum evaporator. The acceleration voltage was set at 10KV during scanning. Microphotographs were taken on different magnification and higher magnification (200X) was used for surface morphology.

In-Vitro Drug Release-

The prepared nanoparticles were evaluated for in vitro drug release by using USP I Basket type dissolution test apparatus. An accurately weighed quantity of formulation (equivalent to 30mg) was filled in capsule and kept in the basket of dissolution apparatus with the dissolution media (900 ml) at 37±0.2C. Samples were withdrawn at a different time interval and compensated with same amount of fresh dissolution media. The Volume of sample withdrawn was made up to 5ml by dissolution media. The samples withdrawn were assayed spectrophotometrically at 242 nm for percentage release of Deflazacort using UV visible spectrophotometer. The release of Deflazacort was calculated with the help of a standard curve of Deflazacort. The scheme of using the simulated fluids at different timing was as follows:

1st hour: Simulated gastric fluid (SGF) of pH 1.2.
2nd and 3rd hour: Mixture of simulated gastric and
Intestinal fluid of pH 4.5.
4th to 5th hour: Simulated intestinal fluid (SIF) of pH 6.8
6th hour and onward: SIF pH 7.5

Drug release kinetic data analysis-

Several kinetic models have been proposed to describe the release characteristics of a drug from the matrix. The following four equations are commonly used, because of their simplicity and applicability. Equation 1, the zero-order model equation (Plotted as cumulative percentage of drug released vs time); Equation 2, the first-order model equation (Plotted as log cumulative percent Drug remaining Vs time); Equation 3, Higuchi's square-root equation (Plotted as cumulative percentage of drug released vs square root of time); and Equation 4, the Korsmeyer-Peppas equation (Plotted as Log cumulative percentage of drug released vs Log time).

Stability studies for optimized formulation-

Stability of a formulation on storage is of great concern as it is the major restraint in their development as marketed preparation. Optimized nanoparticle formulation (F2) were stored in amber colored bottles thus subjected to exhaustive stability testing at 4±1°C and room temperature for 3 month period. Samples were withdrawn periodically and formulation was observed on the basis of % EE, average particle size and physical appearance.

RESULTS & DISCUSSION:

Deflazacort was freely soluble in ethanol, methanol, 0.1 N NaOH & phosphate buffer pH 7.2. and practically insoluble in 0.1 N HCl, distilled water. Identification of Deflazacort was concluded by FTIR spectroscopy with respect to marker compound. It was identified from the result of IR spectrum as per specification in (Figure 1). The calibration curve of Deflazacort was found to be linear in the concentration range of 10-30 µg/ml at 242 nm (Figure 2).

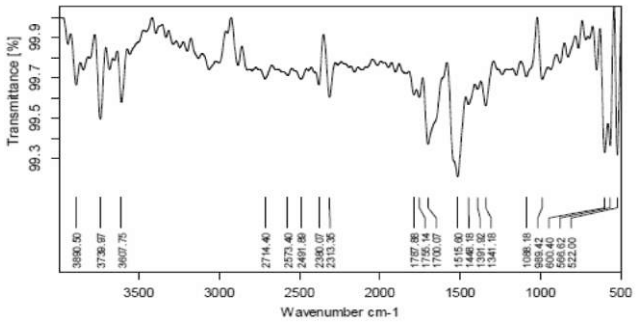


Figure 1: FT-IR Spectrum of Pure Drug (Deflazacort).

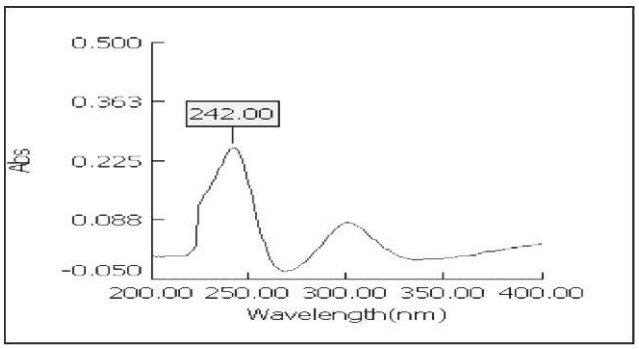


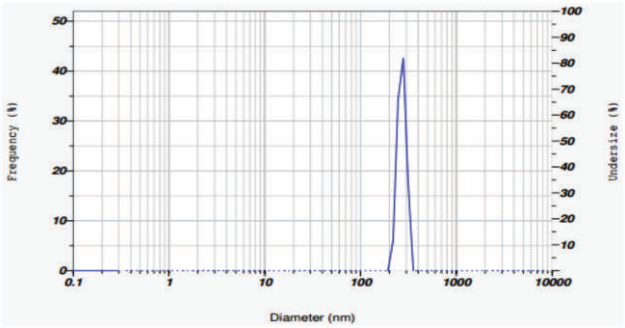
Figure 2: Wavelength maxima of Deflazacort in phosphate buffer pH 7.2

Percentage yield of the different formulation was determined by weighing the nanoparticles after drying. The percentage yield of the different formulation was in the range of 68.89-75.65%. The drug entrapment of different formulations was in the range of 63.23-73.23% w/w. This is due to the mucoadhesion characteristics of chitosan that could facilitate the diffusion of part of entrapped drug to the surrounding medium during the preparation of Deflazacort nanoparticles. The maximum percentage yield and entrapment efficiency were found in formulation F2 (Table 2).

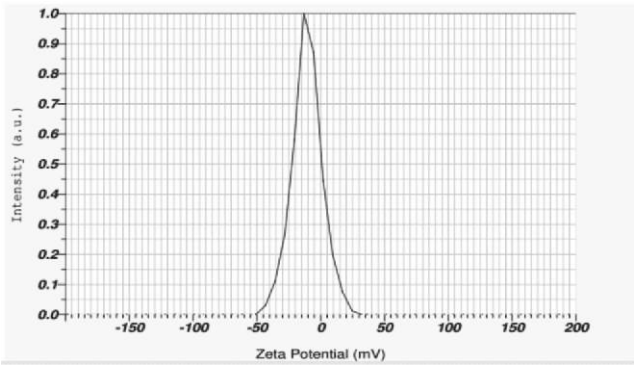
Table 2: Percentage yield and Entrapment efficiency for different formulation.

Formulation	% Percentage Yield	% EE of Nanoparticles
F_1	72.25 ±0.45	65.56 ±0.32
F_2	75.65 ±0.32	73.23 ±0.45
F_3	69.98 ±0.52	70.12 ±0.45
F_4	69.45 ±0.65	68.85 ±0.65
F_5	68.89 ±0.12	65.45 ±0.56
F_6	70.12 ±0.54	63.23 ±0.41

The mean size of the nanoparticles was determined by photo correlation spectroscopy (PCS) on a submicron particle size analyzer (Particle Size Analyzer from Malvern) at a scattering angle of 90°C. The results of measurement of mean particle size of optimized formulation F2 nanoparticles were found 110.23 nm and zeta potential of optimized formulation F2 nanoparticles was found to be -30.5 mV (Figure 3).



(A)



(B)

Figure 3: Particle size (A) Zeta potential (B) of chitosan nanoparticle (F2).

Table 3: Cumulative % drug release of Deflazacort from plain and eudragit S100 coated nanoparticles at different pH.

S. No.	Dissolution medium	Time (hrs)	% Cumulative Drug Release	
			Chitosan Nanoparticle	Eudragit S100 Coated Nanoparticle
1	SGF (pH 1.2)	1	11.25	4.12
2		2	22.25	5.65
3		3	30.12	8.15
4	SGF+SIF(pH 4.5)	4	36.65	9.95
5		5	45.65	12.12
6		6	60.12	22.12
7	SIF (pH 6.8)	7	65.23	38.89
8		8	69.98	45.65
9		9	72.12	60.23
10	SIF (pH 7.5)	10	75.65	70.23
11		12	80.23	82.98

The SEM photomicrographs of the chitosan nanoparticles were taken and characterized in terms of sphericity and particles clumping. As observed in photomicrograph the nanoparticles having a smooth surface and perfectly spherical (Figure 4).

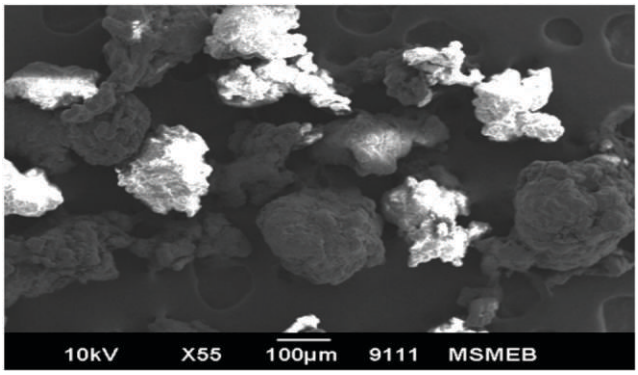


Figure 4: Scanning Electronic Microscopy of optimized formulation (F2).

An *In-vitro* dissolution study was conducted to study the *in-vitro* drug release profile of plain and coated nanoparticle. As the purpose of this formulation was to avoid the release of drug in the gastric and upper intestinal region but to release the drug slowly in the lower part of the intestine maximizing drug concentration in the colon, the *in-vitro* drug release study was conducted at different pH using USP protocol. The obtained results are shown in (Tables 3) while presented in Figure 5 respectively.

The fabricated chitosan nanoparticles were subjected to the study of drug release kinetics and

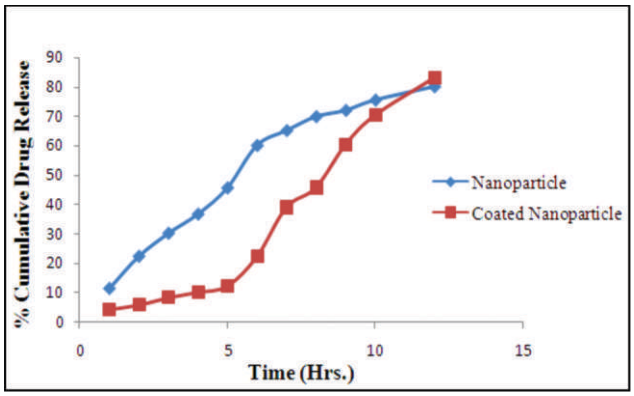


Figure 5: Graph of cumulative % drug release of deflazacort from chitosan and eudragit S100 coated nanoparticles.

release mechanism. The *in-vitro* release data for optimized formulations F2 was analyzed for zero order, Highuchi and Korsmeyer-Peppa's models. Based on the correlation co-efficient (r2) best fitted model was selected (Table 4).

The average particle size of nanoparticle was found 110.23±0.23, 118.56±0.36 and 135.65±0.32 nm after 1, 2 and 3 month of storage at 4.0 ±0. 2°C while at 25-28±2°C the average vesicle size was found 125.32±0.45, 145.65±0.45 and 186.65±0.54 nm after 1, 2 and 3 month of storage. % EE in nanoparticle formulation was 65.56±0.32, 60.54±0.36 and 55.65±0.56% after 1, 2 and 3 month of storage at 25-28±2°C while there were no significant changes in % EE and physical appearance in nanoparticle formulation was observed after 3 month of storage at 4ºC (Table 5).

Table 4: Regression Analysis Data of nanoparticle Formulation.

Formulation	Zero order	First order	Pappas plot
F2	y = 7.644x -14.33	y = -0.053x + 2.126	y = 1.316x + 0.394
	R^2 = 0.905	R^2 = 0.841	R^2 = 0.885

Table 5: Characterization of stability study of Optimized formulation of nanoparticle F2.

Characteristic	Time (Month)					
	1 Month		2 Month		3 Month	
Temperature	4.0 ±0. 2°C	25-28±2°C	4.0 ±0. 2°C	25-28±0. 2°C	4.0 ±0. 2°C	25-28±2°C
Average particle size (nm)	110.23 ±0.23	125.32 ±0.45	118.56 ±0.36	145.65 ±0.45	135.65 ±0.32	186.65 ±0.54
% EE	73.23 ±0.23	65.56 ±0.32	71.45 ±0.54	60.54 ±0.36	69.98 ±0.45	55.65 ±0.56
Physical Appearance	Normal	Normal	Normal	Normal	Normal	Normal

CONCLUSION:

The data generated as an outcome of this article demonstrates that the stable colon targeted Eudragit S–100 coated deflazacort nanoparticles with chitosan for the treatment of IBD was developed. The successful preparation of nanoparticles was established by characterization analysis. The maximum percentage yield and drug content was found 75.65±0.32 and 73.23±0.45 respectively in formulation F2. The lowest particle size entrapped the higher drug content as compared to the other formulations. Also *in vitro* studies of uncoated and eudragit S100 coated nanoparticles was carried out in simulated gastrointestinal fluid medium of different pH. Cumulative percentage drug released was found from various optimized formulation at different time intervals. In case of chitosan coated nanaoparticles nearly 36.65–45.65% of the drug released in initial 4–5 h. This situation is best suited in condition where drug is required to be absorbed or remain in the upper part of GIT. As far as treatment of colonic disease is concerned, it is important to ensure the delivery of drug in intact form in the vicinity of target organ.

REFERENCES:

1. Joshi N, Rajeshwari K. Deflazacort, J Postgrad Med. 2009;55(4):296–300.
2. Markham A, Bryson HM. Deflazacort. A review of its pharmacological properties and therapeutic efficacy, Drugs. 1995;50(2):317-33.
3. Patel SR, Nayak GU, Harsha KP. Deflazacort, Asian Journal of Ear, Nose & Throat. 2011; 1-12.
4. Mayyas MA, Remawi Al. Properties of chitosan nanoparticles formed using sulphate anions as crosslinking bridges. Am J Appl Sci. 2012;9:1091-1100.
5. Zohri M, Gazori T, Mirdamadi S, Asadi A, Haririan I. Polymeric nanoparticles: Production, applications and advantage. IJNT. 2009; 3:1-14.
6. Coco R, Plapied L, Pourcelle V, Jérôme C, Brayden DJ, Schneider YJ, *et al*. Drug delivery to inflamed colon by nanoparticles: Comparison of different strategies. Int J Pharm. 2013; 440: 3-12.
7. Viscido A, Capannolo A, Latella G, Caprilli R, Frieri G. Nanotechnology in the treatment of inflammatory bowel diseases. J Crohns Colitis. 2014; 8: 903-18.
8. Pichai MVA, Ferguson LR. Potential prospects of nanomedicine for targeted therapeutics in inflammatory bowel disease. World J Gastroenterol. 2012;18:2895-901.
9. Antoniou J, Liu F, Majeed H, Qi J, Yokoyama W, Zhong F. Physicochemical and morphological properties of size controlled chitosan-tripolyphosphate nanoparticles. Colloids and Surfaces A: Physicochem. Engineering Aspects. Elsevier Sciences. 2015; 465:137-46.
10. Dubey R, Dubey R, Omrey P, Vyas SP, Jain SK. Development and characterization of colon specific drug delivery system bearing 5-ASA and camylofine dihydrochloride for the treatment of ulcerative colitis. J Drug Target. 2010;18(8):589–601.
11. Guan J, Cheng P, Huang SJ, Wu JM, Li ZH, You XD, et al. Optimized preparation of levofloxacin-loaded chitosan nanoparticles by ionotropic gelation. Physics Procedia. 2011; 22:163-69.
12. Kumar J, Newton AMJ. Rifaximin - Chitosan Nanoparticles for Inflammatory Bowel Disease (IBD). Recent Patents on Inflammation & Allergy

Drug Discovery. 2017;11(1):41-52.
13. Gawde P, Agrawal S. Design and Characterization of Eudragit coated Chitosan Microspheres of Deflazacort for Colon Targeting. J Pharm Res. 2012;5(9):4867-4870.

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Primary Ovarian Pregnancy – A Rare Case Report

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Case Report

ABSTRACT

A pregnancy confined to ovary accounts for upto 3% of all ectopic pregnancy and is the most common type of nontubal ectopic pregnancy.Ovarian ectopic can present as atypical presentation such as adnexal mass. A 26yr old female G4P2L1A1 presented in Gynaecology OPD with chronic dull aching generalized abdominal pain on and offsince 5 months. Occasionally pain would radiate to the right shoulder. There was no history of amenorrhoea, syncopal attack and her menstrual cycles were normal. Patient was admitted and all necessary and emergency investigations were carried out. An ovarian ectopic pregnancy was found (fullfilling the Spiegelberg criteria) after exploratory laparotomy was performed.

KEY WORDS: adnexal mass, ectopic, ovarian, spiegelberg

INTRODUCTION:

A Pregnancy confined to the ovary accounts for upto 3% of all ectopic pregnancy and is the most common type of non tubal ectopic pregnancy. Unruptured ovarian ectopic is rare and is diagnosed if four clinical criteria are fulfilled outlined by Spiegelberg: 1) Ipsilateral tube is intact and distinct from the ovary; 2) Ectopic pregnancy occupies the ovary; 3) Ectopic pregnancy is connected by the utero-ovarian ligament to the uterus and 4) Ovarian tissue can be demonstrated histologically amid placental tissue.

11 per 1000 pregnancies are ectopic out which 95% are tubal and 5% are Non tubal. Non tubal ectopic pregnancy is very rare but potentially life threatening. It is often misdiagnosed and can have rare presentations.

CASE REPORT:

A 26yr old female G4P2L1A1 presented in Gynaecology OPD with chronic dull aching generalized abdominal pain on and off since 5 months. Occasionally pain would radiate to the right shoulder. There was no history of amenorrhoea, no history of syncopal attack and her menstrual cycles were normal. Patient gave history of intake of unsupervised MTP pills since past 5 months at the gestation period of 6 weeks. She gave history of suction and evacuation done at some private setup for uncontrolled bleeding, however no records or ultrasound report were available. After suction and evacuation patient stopped bleeding and resumed her regular menses.

On admission at our hospital, patient was clinically and haemodynamically stable. Per Abdomen Examination-Vague discomfort was felt on whole abdomen. Per Speculum Examination- Cervix grossly normal. Per Vaginal Examination- Uterus anteverted, normal size, mobile, an irregular mass of approximately size 4.3cm felt in the posterior fornix tender and fixed, no cervical motion & tenderness (Figure 3 & 4).

Investigations:

UPT – Positive, Hb-7.9g/dl, Beta HCG-271.60mIU/ml, CA-125-114.40U/ml. Ultrasonography – Heterogenous solid cystic mass lesion seen closely adherent to right ovary of size 5.5*2.8cm showing mild vascularity.

Hospital Course and Management:

After taking written and informed consent and blood arranged, patient was taken for exploratory laparotomy. There was intact pregnancy sac in the right ovarian fossa which was in the process of expulsion (Figure 1). Uterus and both tubes were normal and away from the mass. Gestational sac over the ovary, was removed gently (Figure 2). Corpus Luteum was on right ovary itself with bleeding surface. Haemostatic sutures were applied to the site (Figure 3). Few blood clots of 150 ml were removed from Pouch of Doughlas. Post

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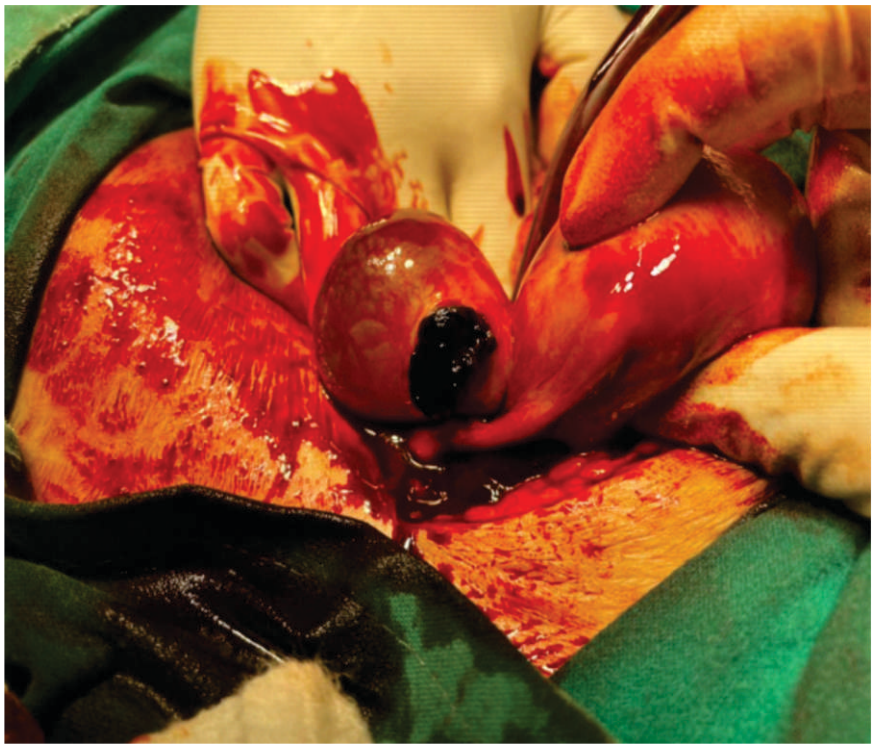

Figure1: Showing Intact sac in process of Expulsion.

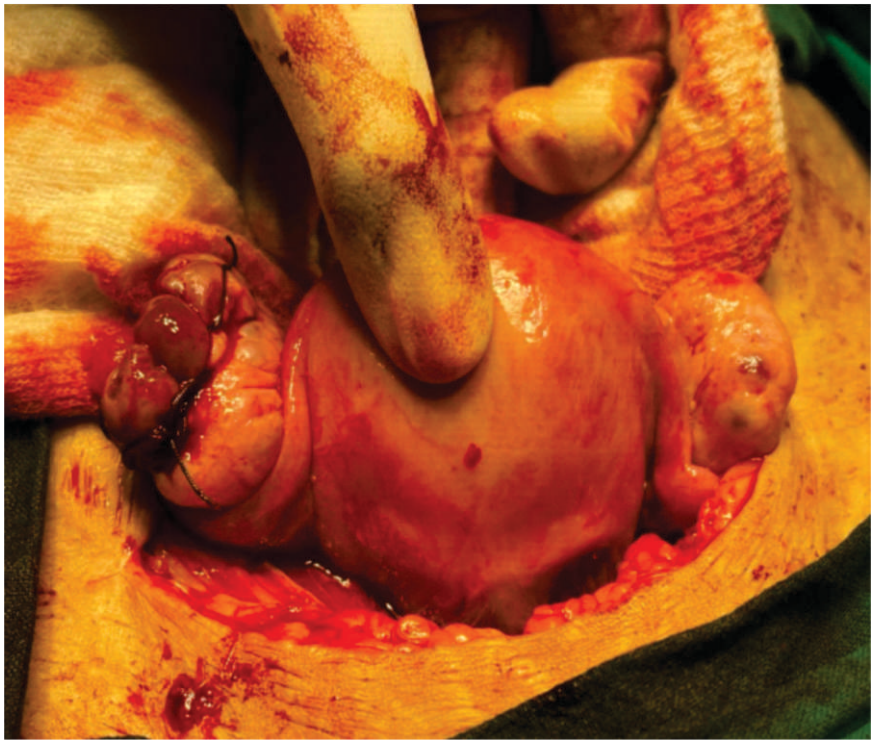

Figure 2: Intact Bi lateral tubes and ovaries.

operatively single unit of blood was transfused. Patient. withstood procedure well. Histopathology report suggests Chorionic villi within the ovarian stroma suggestive of an varian pregnancy (Figure 4).

DISCUSSION:

Ovarian pregnancy is a rare variant of ectopic pregnancy and can have rare presentation of Adnexal mass. Early diagnosis of ovarian pregnancy is necessary in order to avoid more serious complications

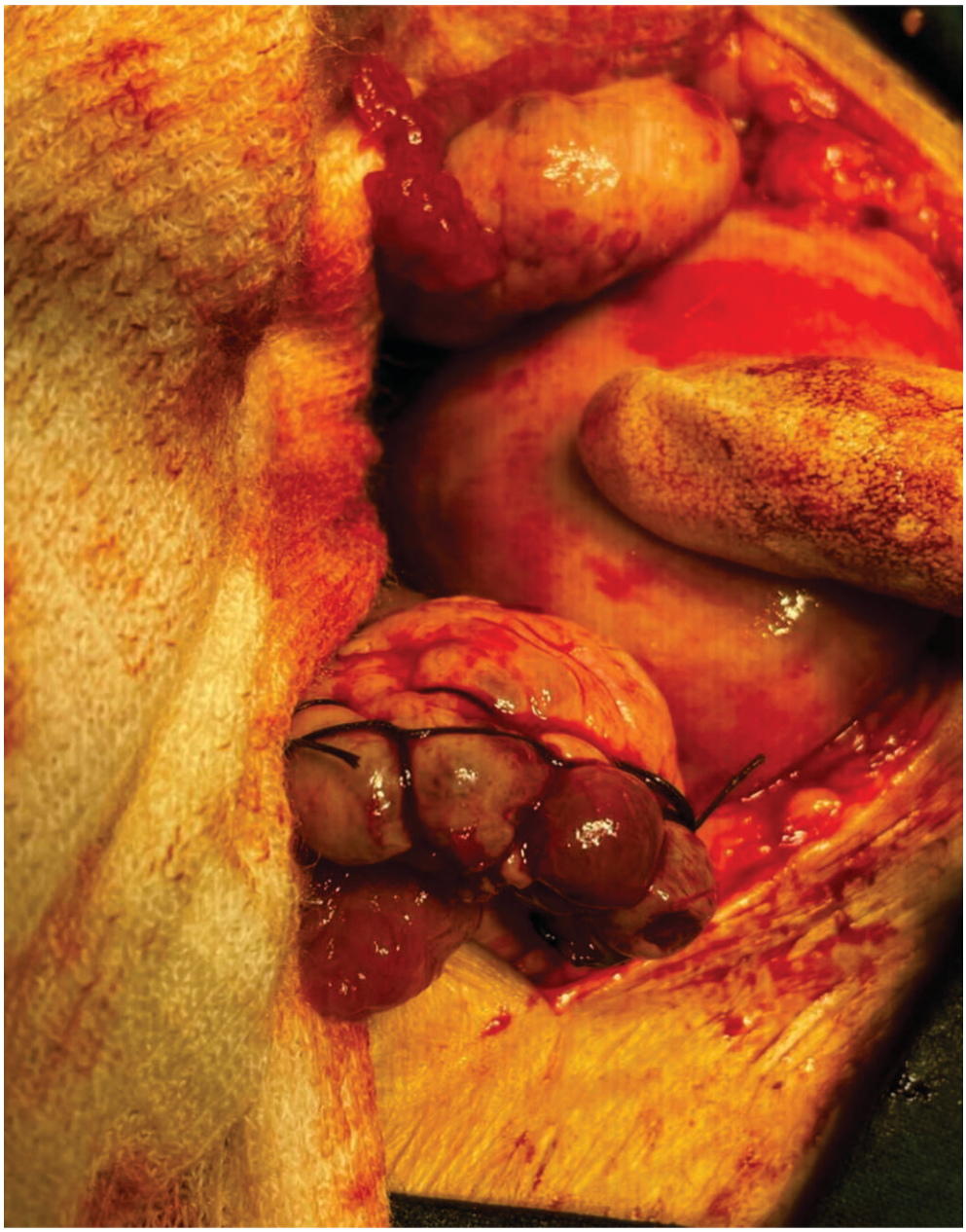

Figure 3: Hemostatic suture applied over ovary.

and emergency invasive procedures.

However, preoperative diagnosis remains challenging. Its diagnosis is difficult and relies on criteria based on intraoperative findings and histopathology report. Its management remains surgical therapy despite the progress in medical treatment.

CONCLUSION:

High Index of suspicion of ectopic pregnancy should be there in women of reproductive age group presenting with ammenohoea. Safe abortion practices to be encouraged and confirmation of location of gestation should be done prior to prescribing medical abortion.

REFERENCES:

1. Bouyer J, Coste J, Fernandez H, Pouly JL, Job-Spira N. Sites of ectopic pregnancy: a 10 year population-based study of 1800 cases. Hum Reprod. 2002; 17(12): 3224-30.
2. Lurie S. The history of the diagnosis and treatment of ectopic pregnancy: a medical adventure. Eur J Obsiet Gynecol Reprod Biol. 1992; 43(1): 1-7.

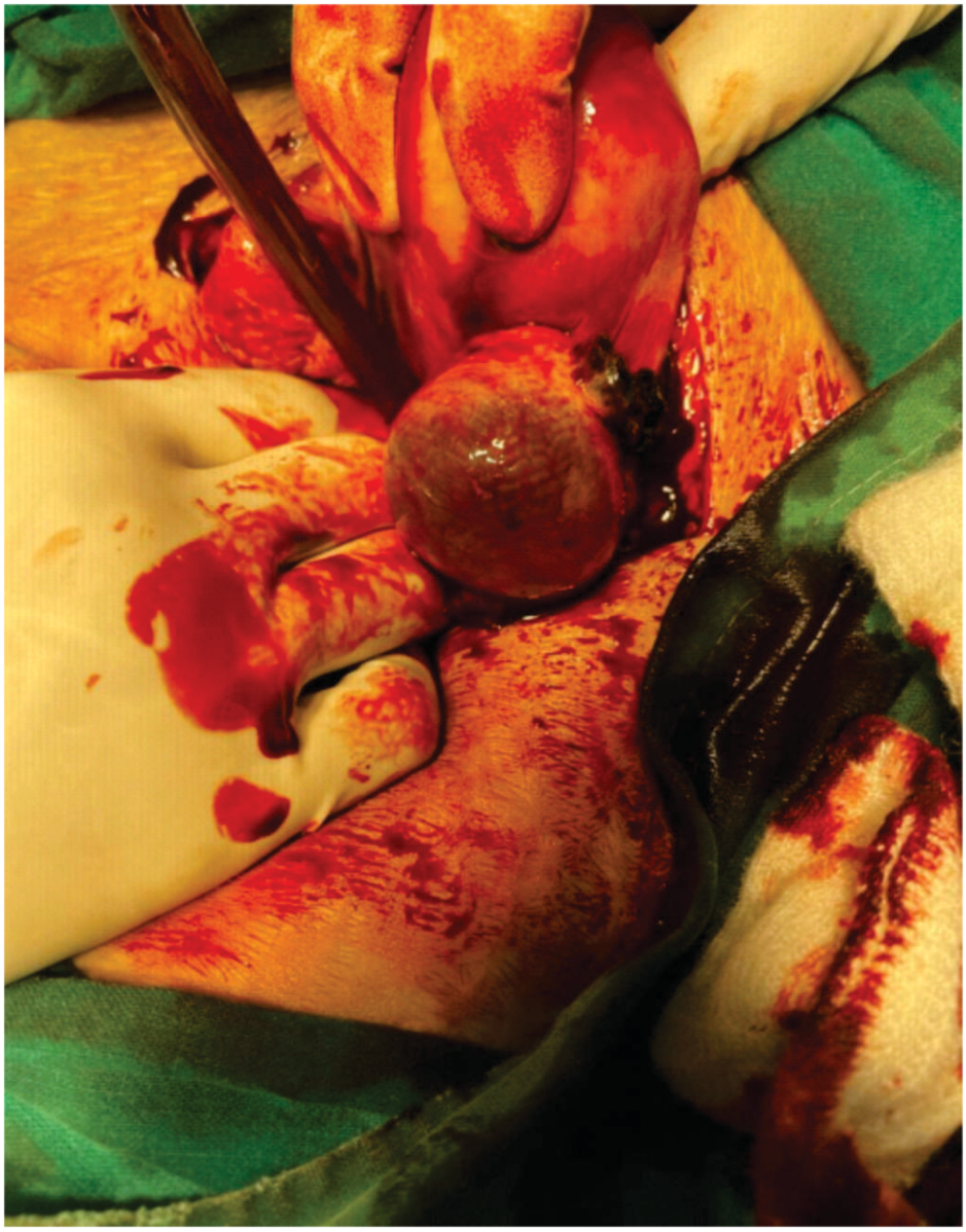

Figure 4: Intact Gestational sac.

3. Gerin-Lajoie L. Ovarian pregnancy. Am J Obstet Gynecol.l 1951;62(4):920-9.

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